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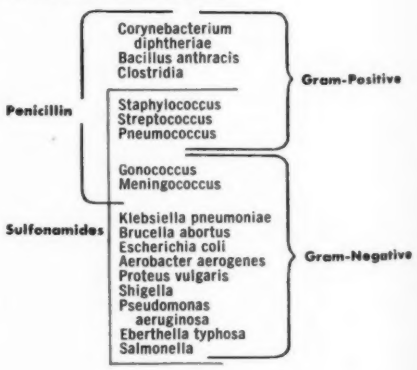

Postgraduate Medicine

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OFFICIAL JOURNAL OF THE INTERSTATE POSTGRADUATE MEDICAL ASSOCIATION

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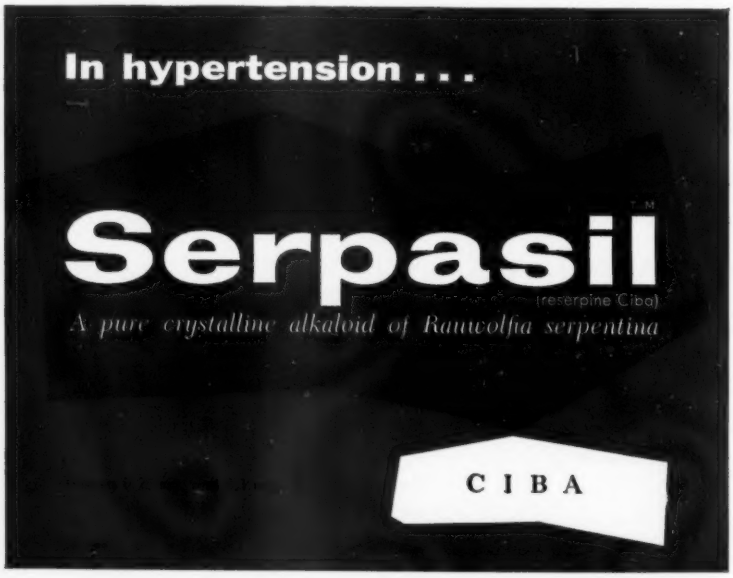

Ocular Manifestations of Carotid-Cavernous Fistulas

A. J. ELLIOT*

Toronto General Hospital and University of Toronto, Ontario

THE SCHNEIDER FOUNDATION EYE PRESENTATION

DR. HENRY G. LANGWORTHY: Twenty-eight years ago, the late Dr. Joseph Schneider of Milwaukee, Wisconsin, left to the Interstate Postgraduate Medical Association a sum of money to administer, the income from which was to be expended for research on constitutional diseases and their relationship to the eye.

In presenting such a broad subject, many noted ophthalmologists have delivered their messages to these Assemblies.

As Director of the Fund for all these years, I take great pleasure in introducing to you Dr. Alfred J. Elliot, Professor of Ophthalmology, University of Toronto Faculty of Medicine, who will present the special topic selected, which is Ocular Manifestations of Carotid-cavernous Fistulas.

I FEEL greatly honored to be asked to give the Joseph Schneider Research Foundation Lecture. Dr. Schneider was widely known as an ophthalmologist in Milwaukee and was intensely interested in the advancement of the science of ophthalmology and wished to provide wide dissemination of this knowledge. I note that these lectures have been presented before this Association since 1925, and the subjects cover a wide range of useful medical knowledge of interest to general practitioners.

There is no doubt that the ocular manifestations of systemic disease can help the physician solve some of the problems with which he is so often confronted. With this in mind I have chosen to review the ocular manifestations of carotid-cavernous fistulas. As the ophthalmic manifestations of this condition are important, it seemed useful to follow this aspect of these fistulas carefully. The patients I will discuss were admitted to the Division of Neurosurgery in the Toronto General Hospital under the care of Dr. E. H. Botterell during the past 10 years.

Part of a paper to be published jointly with Drs. E. H. Botterell and J. W. Cluff, Division of Neurosurgery, Toronto General Hospital and University of Toronto.

*From the Department of Ophthalmology, Toronto General Hospital and University of Toronto, Toronto, Ontario, Canada.

Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

A. J. ELLIOT

The diagnosis rarely presents difficulty. The combination of history of injury, commonly with fracture of the base of the skull, the pulsating exophthalmos, and the constant bruit which is obliterated with digital carotid compression, are characteristic. In many instances the patient describes noises in the head immediately after the accident. Usually they are more pronounced over the eye, but may be heard over a great part of the head. Exophthalmos usually develops rapidly on the side of the fistula, and within a few days becomes pronounced. Preceding the development of exophthalmos there is often the complaint of a severe headache, and there may be a buzzing noise in the head and ears. There is congestion and thickening of the conjunctiva and of the eyelids.

Figure 1 is an example of the striking ocular manifestations of carotid-cavernous fistulas. The proptosis is marked and there is bulbar chemosis and limitation of movement of the eyeball. The retinal veins are moderately dilated and tortuous and the intraocular pressure is slightly elevated. Corneal sensation is diminished.

Blood from the internal carotid artery flows into the cavernous sinus and ophthalmic veins. The ophthalmic veins become greatly dilated. Transmission of the heartbeat is thereby conveyed to the globe through the orbital veins, which are dilated, accounting for the pulsating exophthalmos.

Venous congestion of the eyelids, engorgement of the retinal veins and, occasionally, papilledema are explained on the basis of inadequate venous drainage. There is tremendous dilatation of the venous system within

FIGURE 1 *(Case 1)*. Left carotid-cavernous fistula showing proptosis and bulbar chemosis.

the orbit and adjacent venous channels. Retinal hemorrhages are frequently present and are usually superficially situated. In long-standing cases there is likely to be some degree of optic atrophy. The position of the cranial nerves accounts for their frequent involvement. The sixth nerve is most often affected, possibly because of the free position of the nerve in the cavernous sinus.

Arteriography frequently shows the direct communication between the internal carotid artery and the cavernous sinus, also the retrograde flow of the dye into the ophthalmic veins into the orbit.

When a carotid-cavernous fistula occurs, the pressure within the internal carotid artery and that within the cavernous sinus must tend to become equalized, so that the resultant pressure at the site of the fistula is below the general arterial pressure. Consequently, it is reasonable to assume that blood will be forced from all the collateral arteries toward the fistula. This may even involve a reversal of flow in the ophthalmic artery, which will now be fed by way of anastomosis. Anatomically this point in vascular physiology has actually been observed. There is a collateral circulation existing in many individuals between the external and internal carotid systems, and anastomosis is frequently present between the middle meningeal and ophthalmic arteries and occasionally also between the facial arteries and the ophthalmic artery. Singleton[1] noted the abnormal anastomosis between the middle meningeal and ophthalmic arteries. These points are important in understanding the vascular physiology in connection with the treatment of this disease.

The retinal arteries, being end arteries, do not have anastomoses, and hence the pressure within them must drop considerably. It is evident that the venous pressure within the cavernous sinus must be higher at the site of the fistula than the general venous pressure, so the ophthalmic veins and their tributaries will be subjected to a higher back pressure. Severe congestion must result, and a reversal of venous flow is by no means unlikely. In the retina it would seem probable that decrease in arterial pressure, combined with increase in venous pressure, would result in a highly unsatisfactory supply of blood. This may explain the visual impairment.

Although 10 cases comprise this clinical study,[2] only two will be detailed here in order to bring out the important ophthalmic manifestations which occur during the course of the disease. In the first patient there was an excellent result, but the second patient lost her eye from one of the serious complications.

Case 1—J. S., a minister age 40, was injured in a motor vehicle collision on June 29, 1949. There was retrograde amnesia for three hours and post-traumatic amnesia for one week. Roentgenograms of the skull showed severe fracturing about the left orbit, extending into the right frontal sinus, the ethmoid air cells, and the floor of the right orbit. From the time of regaining consciousness he was troubled by a swishing noise in the left side of his head. Five weeks following the accident, he developed, over a day or two, severe proptosis of the left eye and double vision. Within one week of the onset of the proptosis, pain in the left eye and left forehead became very troublesome.

Examination two months after the injury showed a left pulsating exophthalmos with 10 mm. proptosis of the left eye, severe chemosis and herniation of the conjunctiva. There was a complete left sixth nerve paralysis and a left third nerve paresis, with the left pupil being larger than the right. A continuous bruit could be heard over the left eye, the left frontal and temporal regions. The photograph (figure 1), taken two months after the head injury and before the left internal carotid artery was ligated in the neck, shows the marked proptosis and the bulbar chemosis.

The bruit was obliterated by compression of the left common carotid artery in the neck, but this caused numbness of the hand and dysphasia. A regimen of digital compression was instituted by the neurosurgical service, and nine days later 25 minutes of compression was tolerated without disturbance of cerebral function. On September 1, 1949, the left internal carotid artery in the neck was ligated by Dr. Botterell and the bruit ceased. There was a rapid regression of the proptosis, and

the double vision disappeared approximately six weeks after this operation. At the present time, four years later, the vision in the left eye is 20/20, the pupils are equal in diameter and react normally, the extraocular paralysis has disappeared, and the patient is completely asymptomatic. He appears to have made a complete recovery from his carotid-cavernous fistula.

Case 2—E. C., a 43 year old woman, received a severe blow from a fist across her temple in May 1950. On regaining consciousness two hours later, she was aware of a swishing noise in the left side of the head, which persisted. There was immediate progressive swelling of the orbital contents, with double vision on looking to the left or straight ahead. Within a month she began to develop some proptosis of the left eye and redness of the conjunctiva. Two months prior to admission to the hospital on April 5, 1951, she noticed some swelling of the conjunctiva of the left eye in the mornings, which subsided when she got up and around. At this time she also noted that the right eye was beginning to get red and to become a little more prominent.

On admission to the hospital, bilateral proptosis was present, more marked on the left side. There was moderate injection of the right conjunctival vessels with intense injection of the left eyeball. Moderate edema of the left conjunctiva was present in the mornings and by night it had subsided. Definite pulsation in the left eye was palpable. The left pupil was slightly larger and sluggish in its reaction to light. The visual acuity was 20/30 in the right eye and 20/30 in the left. Double vision was present on looking to the right or to the left or upward. The right fundus was normal; the left fundus showed engorgement of the veins with marked hyperemia of the left optic disk, and a few small, flame-shaped retinal hemorrhages were present in the left eye. A bruit was present over the left eye and left temporal region, which was unchanged by compression of the left common carotid artery, although the patient subjectively noticed a decrease in the amount of noise in the head. The vision in the left eye disappeared completely when the left common carotid artery was pressed, but no numbness in the right hand occurred and no dysphasia was present. The intraocular pressure in the left eye was elevated to 43 mm. Hg, while that in the right eye was 29 mm. Hg. This is an example of one of the complications, the glaucoma that is so frequently present in these patients.

An arteriogram on April 17, 1951, showed evidence of radiopaque dye outside of the internal carotid artery in the cavernous sinus. On May 8, the left internal carotid artery in the neck was exposed by Dr. Botterell and a clamp was applied. It was noted that the blood pressure fell from 175/125 to 80/50. Ligation was deferred for three days, and after this procedure was carried out the patient was noted to be blind in her left eye. Ophthalmoscopic examination revealed massive, radiating, flame-shaped hemorrhages throughout the fundus, and the retinal arteries were almost completely attenuated. It was considered that the collateral circulation was not sufficient to compensate for the increased intraocular pressure, with resulting ischemia and increased permeability of the small retinal capillaries.

On May 13 and 14 she developed a right hemiparesis with some dysphasia. It was then decided to trap the fistula by placing a clip on the internal carotid artery intracranially and on the ophthalmic artery, in order to eliminate the shunt of blood through the fistula which was undermining circulation from the collateral channels. The internal carotid artery was clipped twice intracranially under local anesthesia, and in each instance she became unconscious and the clip was removed. Throughout the day the patient became increasingly hemiparetic and aphasic, and, after considerable consultation and deliberation, it was decided to reopen the neck and remove the sutures from the internal carotid artery. After that, the patient's general condition slowly improved, but the vision in the left eye deteriorated and the intraocular pressure steadily increased until absolute glaucoma developed.

Enucleation of the left eyeball was carried out on August 23, 1951. Pathologic sections

revealed edema of the optic nerve with a large number of hemorrhages in all layers of the retina. In addition, there were many chronic inflammatory cells in the region of the iris root. The delicate balance maintaining the normal intraocular pressure was undoubtedly disturbed, resulting in uncontrollable glaucoma in this case.

This patient has carried on with light housework, although there is a residual partial hemiparesis of the right arm and leg. The dysphagia has disappeared. However, about one year ago the noise on the left side of the head stopped suddenly, and the redness of the right eye cleared up almost immediately. The proptosis of the right eye has gone and the vision is 20/20 with normal fundus findings and intraocular pressure. She had been running a slight increase in pressure in her other eye too. The peripheral and central visual fields are normal in the right eye and there is no chemosis of the left conjunctival socket.

Surgical treatment has been completely unsuccessful in this case. Surgical occlusion of the cervical internal carotid artery resulted in blindness, increasing hemiparesis and dysphasia. Intracranial clipping produced visible and marked spasm of the artery, with loss of consciousness. The circulation of the eye was so disturbed that uncontrollable glaucoma developed and the eye was removed. However, the fistula spontaneously thrombosed about one year ago, resulting in a clinical cure of the condition.

In summarizing this series, the visual results are comparable to those reported by Holman, et al.,[3] in 1951 in a group of 12 patients with carotid-cavernous fistulas. As can be seen from table 1, only 4 of the 10 patients have satisfactory visual results; in the remaining 6 patients, vision was almost completely lost. In one of the latter group the eye was enucleated; that was patient No. 5. Although proptosis remained in 5 patients, it was not a serious complaint except in case No. 3. Glaucoma was noted in 3 patients but was of a low degree, and in only 1 did it become uncontrollable, necessitating enucleation. Optic atrophy was the most common cause of serious loss of vision in these cases. This is probably due to deficient nutrition to the retina from the lowered pressure in the ophthalmic artery.

We believe that vision may be saved in this disease by clamping the ophthalmic artery at the same time as the internal carotid is trapped intracranially. Of course, one might feel that the sight certainly would be lost by

TABLE 1

VISUAL RESULTS IN 10 CASES OF CAROTID-CAVERNOUS FISTULAS

CASE NUMBER	TREATMENT	FOLLOW-UP *(years)*	VISION *Right*	VISION *Left*	PROPTOSIS	EXTRAOCULAR PALSIES
1	Cervical ligation	7	20/20	20/20	5 mm.	None
2	Cervical ligation	4	20/20	20/20	None	None
3	Cervical ligation	4½	Blind	20/20	9 mm.	Partial III
4	Cervical ligation	4½	F. 3 ft.	20/20	2 mm.	None
5	Cervical and intracranial ligation	3½	20/20	Enucleated	None	None
6*	Cervical and intracranial ligation	11	F. 2 ft.	20/20	None	None
7	Cervical and intracranial ligation	5½	None	20/20	4 mm.	None
8†	No surgery	9	20/20	20/20	None	Partial III
9	No surgery	4	20/20	20/20	3 mm.	None
10	No surgery	3	20/20	F. 2 ft.	None	VI

*Operated on by Dr. W. S. Keith.

†Referred to Dr. Botterell by Mr. Joseph Pennybaker, F.R.C.S., The Radcliffe Infirmary, Oxford.

clamping the ophthalmic artery, but I do not think that is the case because of the tremendous collateral circulation that exists between the external carotid system and the internal carotid system. One can inject the common carotid in the neck (and it was done by Walsh[4] 12 years ago and by Elschnig[5] before the turn of the century), having clamped the internal carotid at the same time. On cutting the ophthalmic artery, one will find the solution coming out the distal end of the ophthalmic artery, indicating that adequate collateral circulation exists in the ophthalmic artery between the internal carotid system and the external carotid system.

Hamby and Gardner,[6] in Cleveland, must be given credit for first suggesting in 1933 the clipping of the ophthalmic artery in order to develop an entirely new ophthalmic circulation and to save the eye in the treatment of carotid-cavernous fistulas. Adson's[7] three cases bear testimony to the safety of this procedure, although he had in mind preventing retrograde flow through the ophthalmic artery in order to stop all flow through the carotid-cavernous fistula. For the same reason, Dandy[8] followed Adson in advocating clipping of the ophthalmic artery when intracranial ligation of the internal carotid artery was carried out. In a 1939 report, Singleton[1] noted that the fistula may remain patent if the ophthalmic artery is not trapped.

Table 2 shows the residual ocular findings in our cases at the present time. The extraocular palsies which were present early in the development of the condition disappeared in all of the surgically treated cases except case No. 3, and the partial third nerve palsy in this patient did not annoy him in view of the cataract in the affected eye.

Of the patients who were not treated surgically, one has a partial third nerve palsy and the other a sixth nerve paralysis.

Looking over the table, one can see that less than half of the patients have satisfactory visual results, which, of course, offers a challenge in the treatment of this disease. Proptosis is present in about half of them. Glaucoma is present in at least one-third of the patients, and that corresponds with the series of other individuals in other centers. Optic atrophy is certainly the most common cause of the direct loss of sight. I think that perhaps optic atrophy can be prevented. Complicated cataracts and extraocular palsies are, of course, other ocular manifestations.

TABLE 2

RESIDUAL OCULAR FINDINGS IN 10 CASES OF CAROTID-CAVERNOUS FISTULAS

Vision normal	4
Vision lost or defective	6
Proptosis	5
Raised intraocular pressure	3
Optic atrophy	4
Complicated cataract	1
Extraocular palsy	3

In conclusion, it can be seen that the visual complications of carotid-cavernous fistulas are serious in that blindness, proptosis and ocular paralyses are frequent. It is hoped that these serious visual complications may be less frequent in the future, with a better understanding of the vascular dynamics in the region surrounding a carotid-cavernous fistula.

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Hemorrhage; Number One Problem in Obstetrics

JOHN H. RANDALL*

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Bleeding during and after the third stage of labor has become the most important cause of maternal deaths. Most of the serious cases of postpartum bleeding are the result of severe lacerations of the birth canal and the retention of placental tissue. Much can be accomplished by eliminating traumatic deliveries and by more active management of the third stage of labor.

J. H. RANDALL

DURING the past decade there has been a marked decrease in maternal mortality. This has been due to many factors, such as improved methods of anesthesia, greater availability of blood, the more widespread use of antibiotics and increased hospital facilities. Although there has been a significant reduction of maternal mortality due to puerperal infection and toxemia of pregnancy, there has not been a corresponding decrease in deaths due to hemorrhage. In 1930 there were 251 maternal deaths in Iowa and 25 of these (10 per cent) were due to hemorrhage in late pregnancy, while in 1952 there were 32 deaths and 12 (37.5 per cent) were from the same cause (table 1). Thus, hemorrhage has become the most important cause of death from childbearing. For every 5500 patients delivered in 1952, one mother was needlessly sacrificed because of hemorrhage. No patient in 1952 lost her life from placenta previa or abruptio placentae. It is hemorrhage during and after the third stage of labor that is taking so many lives. Certainly, what is happening in the state of Iowa is much the same as over the entire country, for the quality of obstetrics practiced in this state is on the same level as that in other areas.

Hemorrhage during and after the third stage is usually due to mismanagement of the conduct of labor. It is advisable to give every parturient 0.2 mg. of ergonovine intravenously after the anterior shoulder of the baby stems or immediately following the delivery of the baby. The use of an oxytocic at this time, its mode of administration, and the method of delivering the baby are all controversial. From this procedure many clinics[1] have reported a decrease in the incidence of

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Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

TABLE 1

MATERNAL DEATHS IN IOWA

CAUSE OF DEATH	1930	PERCENTAGE	1952	PERCENTAGE
Toxemia	60	23.9	6	18.7
Abortion	59	23.5	2	6.3
Puerperal infection	41	16.3	0	0.0
Hemorrhage	25	10.0	12	37.5
Other causes	66	26.3	12	37.5
TOTAL	251	100.0	32	100.0

postpartum hemorrhage due to uterine atony. It would not prevent hemorrhage due to lacerations or retention of placental tissue. Some feel that it increases the number of manual removals of the placenta. It is doubtful if this is true, but even if it did it is not a severe enough complication to offset its value of preventing bleeding. From table 2 it can be seen that there has been a decrease in the number of postpartum hemorrhages at the University of Iowa Hospitals during the years 1946 to 1952. This has been the result of two things, the greater use of intravenous ergonovine and the employment of a plan of more active treatment of the third stage of labor. During the same years the incidence of retained placenta was 0.4 per cent which does not seem to be excessive.

After the birth of the baby, ergonovine produces strong uterine contractions and retraction, causing the placenta to separate within a few minutes. When the uterus has changed its shape from a flattened discoid to a more spheric organ (Calkin's sign) the placenta has separated and can be delivered by exerting downward pressure on the fundus. However, if bleeding occurs the placenta should be delivered at once, even if manual removal is necessary. In our clinic the placenta is removed manually whenever there is significant hemorrhage or after a third stage of 20 minutes even if there is no bleeding.

If the patient bleeds following the third stage, the uterus should be brought up out of the pelvis and massaged against the sacral promontory. Often when the uterus is massaged it is pushed down into the pelvic cavity. This obstructs the venous flow from the uterus and promotes further bleeding. If massage does not prevent bleeding the lower birth canal should be inspected for lacerations. In doing this, the upper vagina should be exposed with retractors and the cervix pulled down with ring or sponge forceps. If no source of bleeding is found, a hand should be inserted into the uterine cavity to make certain placental fragments have not been left behind and to feel for any rupture in the uterine wall. The next step to prevent bleeding is to pack the vagina and uterine cavity solidly with gauze. The effectiveness of packing is controversial, but there is little harm from the procedure and it probably does some good. However, packing more than once is to be condemned, because it will usually be ineffective and will cause additional trauma to

TABLE 2

INCIDENCE OF POSTPARTUM HEMORRHAGE

YEARS	NUMBER OF VAGINAL DELIVERIES	NUMBER OF HEMORRHAGES	PERCENTAGE
1926-1935	5,495	257	4.6
1936-1945	12,248	640	5.2
1946-1952	6,827	305	3.1

TABLE 3

ETIOLOGY OF POSTPARTUM HEMORRHAGE

CAUSE OF HEMORRHAGE	NUMBER OF CASES	PERCENTAGE
Uterine atony	579	90.5
Retained placental tissue	29	4.5
Lacerations of birth canal	32	5.0
TOTAL	640	100.0

the lower birth canal. If bleeding continues through the pack, the patient should be subjected to abdominal operation. The uterine arteries should be isolated and ligated, and if this fails to prevent bleeding, hysterectomy should be done.

From table 3 it appears that the most common cause of postpartum bleeding is uterine atony. Much of the hemorrhage due to this cause can be prevented by the routine administration of intravenous oxytocics. Heavy inhalation anesthesia should be eliminated as much as possible, for it greatly increases uterine atony. Most of the severe and fatal hemorrhages are due to severe lacerations of the birth canal, and less commonly to retention of placental tissue. Traumatic deliveries, such as internal version and extraction done under unfavorable circumstances and difficult forceps deliveries, should in this day be discarded in favor of cesarean section done under heavy antibiotic protection. These difficult procedures often lead to severe lacerations which produce uncontrollable hemorrhage.

PITOCIN® stimulation of the uterus during labor has accounted for two uterine ruptures in Iowa during the past year, both of which caused the death of the patient. In our clinic Pitocin is never given to stimulate labor except in cases of true primary uterine inertia and never in the first 24 hours. It is contraindicated in multiparous patients and should never be used when the pelvis of the patient is contracted. The frequent use of intravenous Pitocin in certain clinics to stimulate or to induce labor has encouraged many physicians throughout the country to employ oxytocics without proper control and supervision, with disastrous results in certain instances. Why use Pitocin to initiate labor when a relatively harmless procedure such as the rupture of the membranes is reliable and less dangerous? It is to be predicted that in the future many maternal deaths will result from uterine rupture caused by the use of intravenous oxytocics.

An important part of the treatment of any patient who bleeds during or after the third stage is replacement of blood loss. Intravenous normal saline, 5 per cent dextrose or plasma should be started at once and continued until carefully matched blood becomes available. If unusual bleeding is anticipated, a large bore needle should be inserted into a vein with fluids running and one or two units of matched blood should be on hand before delivery is attempted.

The Maternal Mortality Committee of the State of Iowa has obtained valuable information in reviewing histories of maternal deaths and has come to the following conclusions: Often physicians fail to recognize the exact cause of death, for on death certificates shock, embolism, or heart disease is often listed as the cause of death. In some of these cases the Mortality Committee has judged hemorrhage to be an important contributing factor, if not the primary cause of death.

Naturally, before any remedial steps can be undertaken physicians must realize the importance hemorrhage plays in maternal mortality. Doctors in general underestimate the amount of blood loss, and this is especially true in cases when death has resulted. Too often the patient has to be in shock with increased pulse and lowered blood pressure before the gravity of the hemorrhage is realized. When these signs are present, it is often too late to avoid a catastrophe. Every hemorrhage, regardless of its size, should be seriously considered and steps should be taken at once to discover the cause and to employ effective counter measures. Blood substitutes are being used too freely when blood itself should be employed. They should be used only to tide the patient over until blood is available. A good rule to follow is always to give the patient much more blood than you feel was actually lost. Consultation is often

delayed or neglected entirely when there is severe bleeding. Any hemorrhage which cannot be controlled effectively within a short time demands immediate and competent help. Never is there an occasion when you need assistance more than when you are confronted with a severe postpartum hemorrhage, for such patients can die so easily and quickly. There is a hesitancy on the part of physicians to explore the postpartum uterus when there is bleeding. In years past, when antibiotic drugs and chemotherapeutic agents were not available, it was considered unwise and too dangerous to invade the postpartum uterus until it was absolutely necessary. At the present time, if there is bleeding, it is much safer to palpate the inside of the uterus than to procrastinate.

Antepartum bleeding due to placental separation can be a serious complication of pregnancy and is usually seen after the twenty-eighth week. All patients with vaginal bleeding in this period of pregnancy, regardless of the amount, should be admitted to a hospital for diagnosis and treatment. If there has been considerable bleeding, attention should first be given to blood replacement. Careful abdominal examination often gives some clue as to the type of placental separation. A high, freely movable presenting part or an abnormal presentation such as a transverse lie, are suggestive of placenta previa. A fixed or low presenting part, a tender or rigid uterus, absence of fetal heart sounds, and the presence or history of hypertension should make one think of abruptio placentae.

A more definite diagnosis of the type of placental separation can be made by x-ray methods. A cystogram showing an increased distance between the bladder and fetal head is indicative of placenta previa. This procedure has had a diagnostic accuracy in our hospital of 75 per cent. Soft tissue x-rays, carefully taken and interpreted, will aid in localizing the placenta in at least 80 to 90 per cent of cases. The cervix should always be carefully exposed with a speculum in order to rule out carcinoma, if it has not been previously visualized. From the history and abdominal findings and by careful x-ray procedures, one can usually determine the type and severity of placental separation.

All patients having bleeding from placental separation should be allowed to continue their pregnancy until the baby is of good viable size or until the severity of symptoms demands interference. Patients having a mild degree of abruptio placentae will often stop bleeding after a few days and may go to term, while many of the milder previas can be carried for several weeks before one is forced to terminate the pregnancy. All cases of placenta previa and all patients with abruptio placentae, except the mild ones, should be hospitalized continuously.

When a decision has been made to interrupt the pregnancy of a patient having placental separation, a careful vaginal examination should be done in an operating room set up for cesarean section. The patient should be anesthetized and should be receiving fluids intravenously through a large bore needle. Several units of properly matched blood should be readily available. If vaginal examination reveals a mild degree of previa, the membranes should be ruptured and the patient allowed to deliver vaginally. Partial and complete placenta previas should be treated by cesarean section. No patient with placenta previa should be allowed to labor unless rupture of the membranes effectively and completely controls bleeding. Other methods of treating placenta previa, such as the Voorhees' bag and the bringing down of a leg, are outmoded and should be discarded. The wider use of cesarean section in the treatment of placenta previa has greatly improved both fetal and maternal results. In recent years there has been a tendency to carry patients who have placental separation as long as possible until one is forced to interrupt the pregnancy because of severe bleeding. In some clinics this has decreased the incidence of prematurity and has improved fetal salvage.[2,3]

If vaginal examination reveals no placental tissue in the region of the internal os, the bleeding is due to separation of a normally implanted placenta. The vast majority of these cases can be treated successfully by simple rupture of the membranes. If contrac-

tions do not occur within a short time, Pitocin or PITUITRIN® injections can be given and then discontinued when. regular contractions begin. It is doubtful if an abdominal binder helps a great deal but it does no harm. At the University of Iowa Hospitals 104 cases of abruptio placentae have been treated with only one maternal death which was due to bilateral cortical necrosis of the kidneys. All but four of these were treated by rupture of the membranes alone or associated with Pitocin stimulation and an abdominal binder. There are three indications for cesarean section in the treatment of abruptio placentae: (1) The patient who has concealed hemorrhage and whose uterus does not react to conservative treatment should be delivered through the abdomen. (2) Those patients who are in labor and who have fetal embarrassment during uterine contractions should not be allowed to continue in labor. (3) A few patients who have a severe abruptio placentae develop a bleeding tendency and should be delivered by section.

Bleeding in late pregnancy due to placental separation seems to be quite well managed at the present time. In the University of Iowa Hospitals there have been no deaths from placenta previa and only one from abruptio placentae in the last 10 years. Postpartum bleeding continues to cause many maternal deaths throughout the country and has become the most important contributor toward maternal mortality. Much can be accomplished by eliminating traumatic deliveries, by using Pituitrin more judiciously, and by employing a more active management for the third stage of labor.

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2. MACAFEE, C. G. H.: Placenta previa; a study of 174 cases. J. Obst. & Gynaec. Brit. Emp. 52:313, 1945.
3. JOHNSON, H. W.: The conservative management of some varieties of placenta previa. Am. J. Obst. & Gynec. 50:248, 1945.

MEETINGS and Postgraduate Courses

FOURTH CONGRESS OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE CHEST: June 5-8, Geneva, Switzerland. For reservations write to Professor A. Montandon, Clinique Universitaire d'ORL, Hôpital Cantonal, Geneva, Switzerland.

INTERNATIONAL CONGRESS ON GYNECOLOGY AND OBSTETRICS, GENEVA, SWITZERLAND: July 26-31, 1954. General theme, "prophylaxis in gynecology and obstetrics," will be reported on by 30 to 35 eminent gynecologists from all over the world, with 100 to 120 other speakers enlarging upon and discussing these papers. Scientific and technical exhibits as well as scientific films will be shown. Program of 60 free communications, without translation, is being prepared. For further information apply to the Secretariate of the Congress, Maternité, Geneva, Switzerland.

POSTGRADUATE COURSES ARRANGED BY THE AMERICAN COLLEGE OF PHYSICIANS

WAYNE UNIVERSITY COLLEGE OF MEDICINE, DETROIT: Course in clinical electrocardiography, April 19-24, 1954.

NORTHWESTERN UNIVERSITY MEDICAL SCHOOL, CHICAGO: Course in clinical hematology, April 26-30, 1954.

UNIVERSITY OF PENNSYLVANIA SCHOOL OF MEDICINE, PHILADELPHIA: Course in internal medicine, May 10-14, 1954, at the auditorium of the American College of Physicians.

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE: Course in diseases due to allergic and immune mechanisms, May 17-21, 1954, at the Hotel William Penn, Pittsburgh.

UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL, SAN FRANCISCO: Course in internal medicine, June 14-18, 1954, at the Extension Building.

OHIO STATE UNIVERSITY COLLEGE OF MEDICINE, COLUMBUS: Course in isotopes in clinical medicine, June 14-18, 1954, at the New University Hospital.

UNIVERSITY OF COLORADO, DENVER: Annual Pueblo spring clinic at Pueblo, Colorado, April 3, 1954.
Postgraduate course in obstetrics and gynecology at the Medical Center, April 9-10, 1954.
Western Colorado spring clinic at Grand Junction, Colorado, April 23-24, 1954.
Weld County spring clinics at the Weld County Hospital in Greeley, May 6, 13, 20, 25.
"A Clinical Day in Pediatrics," at the St. Francis Hospital, Colorado Springs, May 19, 1954.
Colorado medical alumni clinics at the Medical Center, June 4, 1954.
Colorado intern and resident clinics, fifth annual sessions, at the Medical Center, June 10-11, 1954.

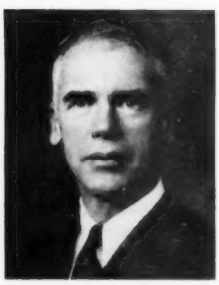
Clinical Experience with Atomic Energy

SHIELDS WARREN*

Harvard Medical School, Boston

Radioactive isotopes may be used therapeutically either internally or externally as radiocobalt, radiophosphorus, radioiodine or radiogold. Their therapeutic uses are being well defined. The industrial medical problems of atomic energy, including civil defense problems related to atomic explosions, are considered together with a clinical discussion of the effects of radiation.

EIGHT years ago atomic energy was almost unknown to all of us. At present it has concerned and is concerning hundreds of thousands of our population and may well concern even more as time passes.



SHIELDS WARREN

There is no opportunity to cover all the aspects of atomic energy that are of importance or of interest to medical groups, so I will simply select three of these.

Therapeutic Use of Radioactive Isotopes

First and perhaps most publicized is the external use of radiocobalt as a substitute for radium in the external and implantation treatment of tumors. Radiocobalt is used exactly as radium is and can be produced at about one-thousandth of the cost of radium, and it can be made many times as radioactive for a given mass as is the naturally occurring radium. It has the disadvantage of a relatively short half-life, so that in utilizing cobalt as a source for the gamma rays desired for treatment purposes, its half-life of only five and a half years makes it necessary to have provision for replacement of at least a portion of the charge.

Three radioactive isotopes have acquired particular popularity for internal use. The

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Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

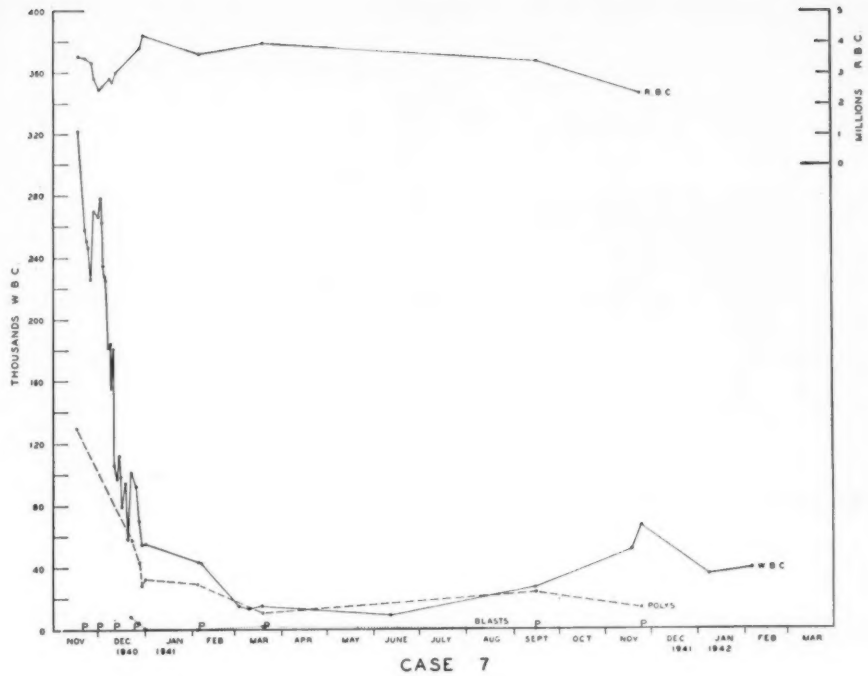

FIGURE 1. Decrease in white count following radioactive phosphorus therapy.

(Reproduced from: Warren, S.: Physiologic effects of nuclear energy. Occup. Med. 2:447-451, 1946.)

first of these, radioactive phosphorus, is the treatment of choice in polycythemia vera. It is also a useful means of therapy in the ordinary types of chronic leukemia.

Figure 1 illustrates the results obtained by treating a patient with chronic myelogenic leukemia and a white cell count of 320,000. After the administration of four doses of approximately 4 millicuries each, there was a striking regression. Further treatment was required at the end of a year, and the patient got along fairly well for a three year period after that. It is not the treatment of choice for leukemia, but it is a useful alternate for some of the other methods of therapy.

Another important isotope is radioactive iodine. Figure 2 shows the treatment of a patient who received a small tracer dose, measured in microcuries (millionths of a curie), with the absorption of the radioiodine in the thyroid indicated. Using four Geiger counters in shielded boxes, it is possible to note the amount of radioiodine localized in the thyroid and the portions of the thyroid in which it is localized, thus obtaining an accurate diagnosis of the activity of the thyroid gland. At present this is perhaps the surest test for determining hyperfunction of the thyroid gland.

Radioiodine can be used therapeutically in several ways. Figure 3 was taken from one of the cases of Dr. Hermann L. Blumgart at the Beth Israel Hospital, Boston, and was chosen to illustrate the fact that the parathyroid is undamaged while the immediately adjacent thyroid has been virtually obliterated by the dose of radioactive iodine given. In this case of severe cardiac involvement it was necessary to ablate the thyroid gland to permit the patient any activity at all.

FIGURE 2. Radioactive counting set-up for cancer of the thyroid.

One can gauge quite accurately the degree of destruction of the thyroid to be attained, and in patients with hyperthyroidism who have any complications, it is a useful treatment.

Another isotope which is quite useful is radioactive gold, which can be injected intraperitoneally or intrapleurally in order to control fluid formation due to metastatic growth.

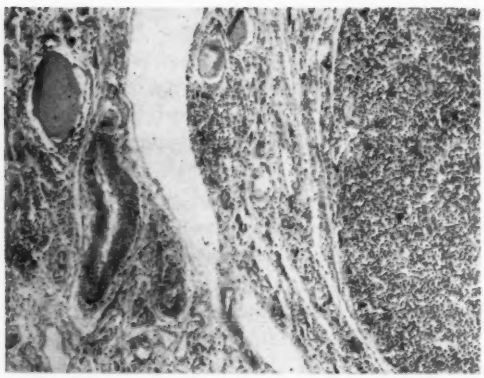

FIGURE 3. Note uninjured parathyroid with almost complete destruction of thyroid.

(Reproduced courtesy of Drs. Hermann Blumgart and A. S. Freedberg, Beth Israel Hospital, Boston.)

The radioactive gold partly attacks the cancerous cells and partly the mesothelial lining of the pleural and the peritoneal cavities so that there will be a cessation, in favorable cases, of serous effusion, which is so troublesome to these patients. From a shielded container, the radioactive colloidal gold, in suspension and diluted with saline, in measured amounts, is forced by the syringe into the peritoneal cavity (figure 4).

The distribution of radioactive gold obtained is shown in figure 5. After the first half-hour the radioactivity is still somewhat localized; at three and a half hours it is quite widespread, and at the end of seven days it is quite evenly spread. There is very little radioactivity left beyond the seven day period, so we need not worry about its distribution after that time.

There are a number of other radioisotopes that can be used for therapeutic purposes, but I will not go into these. As other radioactive isotopes become more widely of value, as certainly they will, we will be able to call them to your attention through the medical journals. There is hardly an issue of the medical journals coming out today without a report of some new use of a radioisotope.

FIGURE 4. Apparatus for administration of radioactive gold peritoneally.

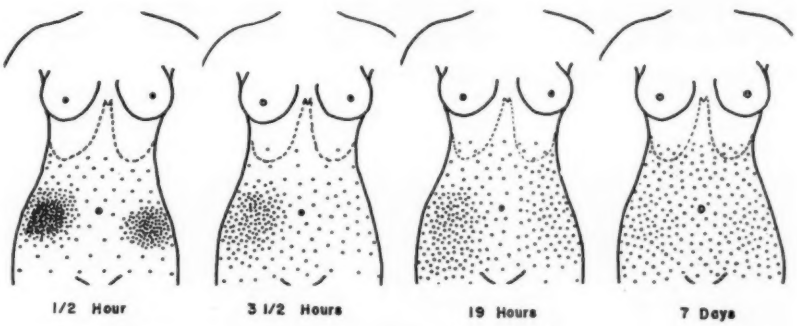

FIGURE 5. Typical pattern of gold distribution in abdomen.

(Figures 4 and 5 reproduced from: Rose, R., Osborne, M. P. and Stevens, W. B.: The intracavitary administration of radioactive colloidal gold. New England J. Med. 247:663-667, 1952.)

Industrial Medicine

The second aspect of atomic energy to which I wish to call your attention is that of industrial medicine and public health. The atomic energy business is big business with literally thousands of employees. You may have seen a recent announcement that there is to be soon set up an experimental atomic reactor for the production of electric power. This will be but a prelude to an even wider industrial utilization of atomic energy.

In any utilization of fissionable material, whether in a sudden explosion or in controlled form for the production of thermal energy or power, radioactive products are formed by the reactions that occur. These radioactive ashes of atomic activity are real hazards that have to be guarded against. Moreover, the manufacture and purification of the materials that are fissionable in themselves, uranium and plutonium, are also hazardous from the

FIGURE 6. Phagedenic ulcers after irradiation leukopenia.

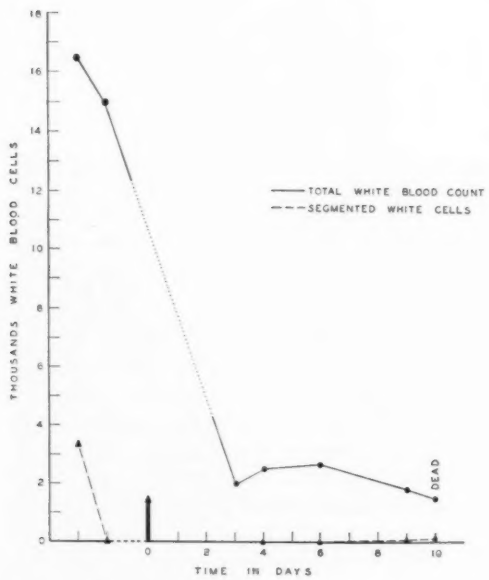

FIGURE 7. Decrease in white count following exposure to ionizing radiation.

standpoint of chronic exposure to radiation.

When we speak of the special hazards of atomic energy we do not mean that they are peculiar hazards. Just as the gasoline industry has the hazard related to lead poisoning from the tetraethyl lead additive, so the atomic energy industry has the problem of radiation from the radioactive materials with which work is done and the radioactive ashes left when that work has been performed.

Fortunately there is a very wide gap between the amount of radioactivity that can be detected and the amount of radioactivity that is harmful. For example, in my wrist watch, which probably has about the same amount of radioactivity as those many of you are wearing, there is a trace of radioactivity. In ordinary circumstances that is completely harmless. On the other hand, if considerable amounts of that radioactive paint were to be ingested, as occurred with the radium watch dial workers in New Jersey some 20 years ago, there would be damage to the blood-forming tissues along with the induction of sarcomas in bone as a result of continued low level exposure to radiation. So long as the activity is controlled—and we have ready means of control by Geiger counters, the electroscope, photographic film, and other means —we can easily check and control the types of exposures to which workmen or others may possibly be subjected, and we can look back with a good deal of pride on the record of the atomic energy industry.

For purposes of comparison, let me recall the radium industry. Nearly a thousand persons were required in the preparation or handling of approximately a pound of radium for medical purposes. Ten per cent of those were seriously injured or died as a result of exposure to the radium. Through the lessons learned from them and from the early radiologists as to the dangers of exposure to radioactive substances, it was possible to set up and to enforce effective standards of safety in the atomic energy program. Consequently, among the hundreds of thousands of people working with the equivalent of many hundreds of tons of radium, there have been only two deaths and a bare handful of nonfatal injuries.

What are the injuries to watch for in the industrial utilization of atomic energy? They are essentially the effects of chronic radiation, and they are manifested in several ways, depending on the character of the radiation and on the degree of exposure to that radiation. If the radiation is external and moderately penetrating, the bone marrow and particularly the white blood cells of the bone marrow are the targets. The danger one has to fear is the development of aplastic anemia or leukemia. From the standpoint of the more penetrating types of radiation, as from radiocobalt and some of the other fission products that give off relatively penetrating radiation, the danger is to the internal organs. If the radiation is soft the damage is to the skin, and radiation dermatitis or radiation carcinoma are the conditions to guard against.

If the material, particularly fission products, is inhaled or ingested, the damage usually occurs after absorption and, again, is to bone marrow or to bone; with some of the less soluble substances the danger is to the lungs themselves.

These hazards are all known, all guarded against, and the degree of protection attained thus far has been very satisfactory in the experience of the Atomic Energy Commission.

When there is still wider use of radioactive materials, the chance of accidental spill will perhaps be greater, although we have learned that by careful training of personnel this can be almost completely avoided. However, it is well for those of you particularly interested in industrial health to keep in mind this new industry, with its associated new, potential—although not actual—hazards.

Civil Defense

The third phase of atomic energy that I wish to mention is one of which every doctor needs to be aware to fulfill his responsibilities from the civil defense standpoint, that is, what he needs to know for the victims of an atomic explosion, whether victims of an accidental explosion or of enemy action. For this purpose I would like to review briefly the salient findings in the Japanese cities of Hiroshima and Nagasaki.

FIGURE 8. Multiple hemorrhages in intestine (official U.S. Navy photo).

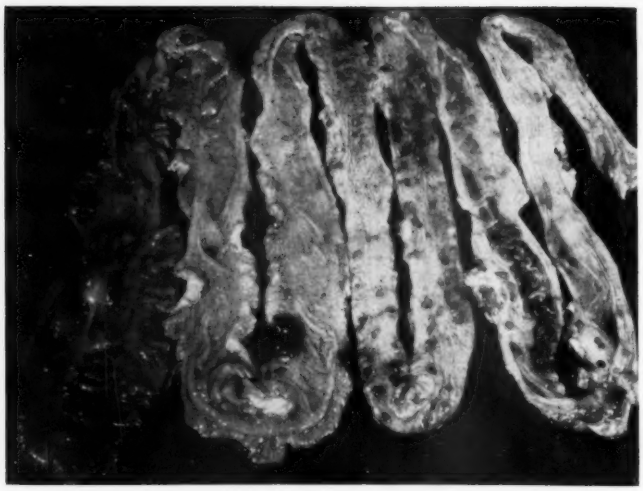

FIGURE 9. Ulceration of intestine following exposure to atomic bomb (official U.S. Navy photo).

(Reproduced from Tullis, J. L. and Warren, S.: Gross autopsy observations in the animals exposed at Bikini. J.A.M.A. 134: 1155-1158, 1947.)

If I can go back with you to August 1945, I would like to present some cases to point out that radiation injuries are not the only problems that you will encounter if there should be an atomic explosion, because there will also be trauma from blasts and burns from the thermal energy. These will be complicated by radiation injuries and many persons who have been sheltered from the direct effects of either blasts or thermal energy will suffer from the acute radiation syndrome.

I cannot tell you anything you do not know about trauma; I cannot tell you anything you do not know about the care of burns, but perhaps I can point out a few things that may be helpful concerning acute radiation syndrome.

The first thing to remember is that the tissues of the body most sensitive to radiation injury are the white blood cells and the bone marrow. Consequently, the very early deaths were those resulting from multiple infection with nonpathogenic organisms (figure 6). The phagedenic ulcers scattered on the skin and the cellulitis of the neck (a vain attempt at drainage had been made) were due simply to the patient's own nonpathogenic bacteria which had taken over because he had no polymorphonuclears. Obviously, in this period, when the white cell count is down or absent, one needs antibiotics to bridge the absence of these cells and to protect against infection.

FIGURE 10. Epilation following exposure to atomic bomb.

We feel that a greater number of those who were bombed would have died had therapy not been available for them.

In addition, we find that the white cell count comes back rather slowly. In a group of experimental animals, chosen for the atomic bomb tests on the Pacific island of Bikini because we could follow them for a long period of time, a very prompt drop of the white cells was noted (figure 7). Of course, many animals died in this period, and their white cell counts went down to zero, but in others it gradually rose for a considerable period of time, coming back to normal at the end of some months. Those Japanese who survived for four to five months after the explosion came back almost entirely to normal and very few have had any trouble since that time. Some developed leukemia; others, because of the radiation effect on their eyes, have developed cataracts, but these are relatively few compared with the large number who have survived. So, by and large, those persons that can be kept alive for four or five months will in all probability do well subsequently.

Next to the problem of the low white cell count and infection is that of the hemorrhagic diathesis which results chiefly from the thrombocytopenia, although hepatic malfunction and disturbances of fibrinogen formation and of the prothrombin and heparin balance come into the picture, as well. Figure 8 gives an idea of the extensive hemorrhages that occur in the gastrointestinal tract (this again from one of our experimental animals at Bikini). There is also tremendous damage to the mucosa of the intestine. This is very important to keep in mind in cases of individuals who may have been exposed to large amounts of radiation and who develop the acute radiation syndrome. These people have been so injured that their intestinal mucosa is in large part gone and it is virtually impossible for them to absorb through their intestines, so they require parenteral fluids, parenteral food, and parenteral medication.

Another example of this hemorrhagic manifestation, which is most prominent from about the fifth day to the sixth or seventh week following exposure, is shown in figure 9.

A patient showing epilation can be seen in figure 10. He was not in the hospital because of the epilation, of course, but because of the pancytopenia that he had. He was tided over and survived with the help of antibiotics and of transfusions. Ultimately, his hair grew back. We have almost no examples of completely and permanently epilated individuals who survived. In general, those who survived were those with only transient epilation.

These examples will serve to recall to your minds some of the symptom complexes of the acute radiation syndrome which may occur alone in the event of an atomic explosion, if individuals have been relatively sheltered from the effects of blasts and fire, or which may be complications of the more familiar types of injuries.

The most important therapeutic points to keep in mind are (1) the control of infection, (2) the replacement of the missing blood cells, (3) the replacement of fibrinogen. Therapy by mouth will be of very little value to the majority of survivors, because their intestinal tracts will be seriously damaged, and they will be nauseated, vomiting and suffering from intense diarrhea.

If there is a combination of burn and radiation injury, patients do much worse than with either alone; that is, a sublethal burn and sublethal radiation when combined will result in a fatal outcome for the patient.

One of the important aspects of the application of these problems to civil defense is this: In all probability, if such a disaster occurs it will be on so large a scale that no one area can look after itself, and there will have to be a considerable number of doctors, nurses, and relief workers brought in from other areas; there will be no opportunity for instruction as to what to do under these circumstances, and it is for this reason that I have ventured to call to your attention the few therapeutic principles that are established at the present time.

Unfortunately, we as yet have no specific agent against radiation, but we are far from helpless, and in the event of a large scale explosion, there is much that you would be able to do to help those still alive to survive.

Present Evaluation and Future Potentialities of Cardiovascular Surgery

JOHN W. KIRKLIN*

Mayo Clinic, Rochester, Minnesota

The conditions of the heart and great vessels amenable to surgical treatment are noted. A brief discussion of several of these is given, including the methods of operative management employed. Finally, an attempt is made to survey the lines along which future progress will be made.

THE glamour that always has attended development of a new field of medicine recently has surrounded cardiovascular surgery. Both laity and physicians have been subjected to glowing descriptions of the miracles accomplished by operations on the human heart. While enthusiastic reports have emanated from some quarters, a few persons have tended to regard such operations as radical and have deprecated attempts to extend surgical endeavors so close to where, by most accounts, lies the soul of man. It is now time that we, as physicians, cease to be swayed unduly by either of these extremes. It is time that we take stock of the field of cardiovascular surgery so that we may know its present status and its future potentialities.

Present Status of Cardiovascular Surgery

In order to assess the present status of this relatively new branch of surgery, it is in order to review briefly the conditions of the heart and great vessels that are amenable to operation. Before noting these, I should like to call to your attention a fact so often emphasized by my colleague, Dr. O. T. Clagett, namely, that cardiovascular surgery is reparative, or physiologic, in nature and is not extirpative. At present it is possible to remove a man's lung, his entire stomach, his hip or his leg. The contents of the pelvis can be excised en bloc. While such operations are necessary and valuable under certain circumstances, they cannot be compared to a procedure in which nothing is removed or destroyed but in which an abnormal opening is closed, an obstruction bypassed or a leak repaired. For

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Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

this reason, cardiovascular surgery must be recognized as being inherently different from destructive surgery.

Many diseases of the heart and great vessels are now being treated by surgical measures (table 1). In many instances an operation of proved value is available for a specific malady. Certain operations, such as those being used in the treatment of aortic and mitral regurgitation and ventricular septal defect, are in developmental stages and cannot be considered of proved value. Many other congenital and acquired diseases of the heart remain as yet invincible against surgical attack.

Results of Cardiovascular Surgery

It is not enough merely to tabulate a list of conditions of the heart and great vessels amenable to operation. A permanent effort in this field can be justified only by a low mortality rate and a high incidence of good results. It is obviously impossible here to review these data for all types of operations on the heart and great vessels. Instead, a brief review of the pertinent facts regarding procedures will be given.

JOHN W. KIRKLIN

Patent ductus arteriosus—In the realm of congenital cardiac disease, a patent ductus arteriosus is a common condition. A patent ductus arteriosus is an abnormal communication between the aorta and the pulmonary artery, through which already oxygenated blood is shunted from the aorta back through the pulmonary circuit. From 20 to 90 per cent of the output of the

TABLE 1

CONDITIONS OF HEART AND GREAT VESSELS AMENABLE TO SURGICAL TREATMENT

- Lesions of the heart
  - Stab wounds
  - Valvular heart disease
    - Mitral stenosis
    - Mitral regurgitation*
    - Aortic stenosis, acquired and congenital
    - Aortic regurgitation*
    - Congenital pulmonic stenosis with intact ventricular septum
    - Tricuspid stenosis
    - Tricuspid atresia, congenital
  - Atrial septal defect
  - Ventricular septal defect*
  - Coronary artery disease*
  - Tetralogy of Fallot
- Lesions of the pericardium
  - Traumatic hemopericardium
  - Chronic constrictive pericarditis
- Lesions of the great vessels
  - Anomalous pulmonary venous connections
    - Partial
    - Complete*
  - Patent ductus arteriosus
  - Partial persistent truncus arteriosus (aortic-pulmonic fistula)
  - Coarctation of the aorta
  - Congenital "vascular rings"
  - Aortic aneurysms
    - Thoracic aorta
    - Abdominal aorta
  - Complete transposition of the great vessels*
  - Thrombotic occlusion of the abdominal aorta*

*Operation still in developmental stage.

left ventricle is thus rerouted back through the lungs, depriving the body of this amount of blood and severely straining the left ventricle. Rarely does a person who has this defect live to the age of 50 years. Left ventricular failure, the onset of pulmonary hypertension and rupture of aneurysmal dilatations in the region of the patent ductus arteriosus all take their toll of lives, so that most untreated patients die in late childhood or early adult life. Some patients who have patent ductus arteriosus die of cardiac failure even in the first few months of life. Unquestionably, this is a serious form of congenital cardiac disease.

Thanks to the pioneering efforts of Gross,[1] patients who have patent ductus arteriosus no longer need succumb to this malformation. It is now an accepted practice to recommend operation in all cases of uncomplicated patent ductus arteriosus, whether or not symptoms are present, because of the known poor prognosis in this condition. The patent ductus arteriosus is carefully dissected out at operation. If the ductus is long, pliable and relatively narrow, I have closed it by the multiple suture-ligation technic described by Blalock.[2] If the ductus is short, thick or sclerotic, such a technic will not, in my opinion, assure complete and permanent closure. In such instances, division of the patent ductus arteriosus is performed.[3]

It is proper to inquire as to the results of operation in uncomplicated patency of the ductus arteriosus. This must be known because the physician can recommend operation for a youngster who has patent ductus arteriosus only when he is armed with knowledge about the benefit of such an operation. The operative mortality rate in the experience at the Mayo Clinic and in that of other surgeons working in this field is approximately 2 per cent.[4] All patients surviving operation for uncomplicated patency of the ductus arteriosus are truly cured, for this is one of the few surgical procedures in which an abnormal situation is converted into a completely normal one by operation. It must thus be considered a perfect surgical procedure.

Coarctation of the aorta—This condition is a congenital narrowing of a portion of the aorta of such dimensions that severe obstruction is present to the flow of blood through the coarctate zone. Hypertension with all its serious sequelae develops in the upper part of the body. The coarctation is most commonly situated in the upper part of the thoracic aorta just distal to the origin of the left subclavian artery.[5] Most patients who have coarctation of the aorta die as a result of this disease before the age of 35 years.[6] Thanks to the pioneering work of Crafoord and Nylin[7] and of Gross and Hufnagel,[8] surgical repair of this lesion is possible. It is now my practice and that of my colleagues to advise operation for all patients who have uncomplicated coarctation of the aorta.

At the time of operation, the entire upper portion of the thoracic aorta must be carefully but completely mobilized. This is done with complete precision, for the large, thin-walled intercostal arteries that have developed to produce collateral circulation around the coarctation bleed furiously when inadvertently damaged. With care, however, the dissection can be effected safely. After appropriate clamps have been placed, the coarctate portion is excised, and an end-to-end anastomosis is made between the two ends of the aorta. The stoma at this line of sutures should be as large as the aorta itself, else a perfect result may not ensue.

It is revealing to compare the results of operation for coarctation of the aorta[9,10] with the results of operation for another serious disease, namely, carcinoma of the stomach.[11] This comparison is not entirely fair, because the operation for repair of coarctation has been performed for only about eight years, and thus the number of patients who were operated on five years ago or more is limited. Realizing the statistical unreliability of a comparison of the figures, I find them none the less revealing (table 2). These figures are not presented to decry the results of operation for carcinoma of the stomach but to emphasize that in certain cardiovascular malformations, such as coarctation of the aorta, an operation of seemingly great magnitude can be performed with safety by a team experi-

enced in this type of work. More important, once the patient who has uncomplicated coarctation has survived a satisfactory operation, he is virtually assured of normal life expectancy.

Arteriosclerotic aneurysm of the abdominal aorta—Patent ductus arteriosus and coarctation of the aorta are congenital anomalies that demand treatment in childhood or early adult life. Other cardiovascular lesions that are likewise urgently in need of correction may appear later in life. Arteriosclerotic aneurysms of the abdominal aorta may occur during the sixth and seventh decades of life. They present themselves as pulsating abdominal masses that may be otherwise asymptomatic when first noted. Sooner or later, severe discomfort develops; finally, rupture and death bring relief to these miserable patients. The prognosis with regard to life expectancy is notoriously poor for persons who have such aneurysms (table 3).

Because of this known poor prognosis and because asymptomatic aneurysms have been associated with as poor a prognosis as symptomatic ones, my associates and I[12] advise operation for all persons who have arteriosclerotic abdominal aortic aneurysms. Following the work of Dubost and co-workers,[13] Bahnson,[14] DeBakey and Cooley[15] and others, we have abandoned all forms of treatment with the exception of resection and replacement of the aneurysm with a preserved homologous aortic graft.

In a small experience, embracing the insertion of homografts into the abdominal aorta on eight occasions, we have had no deaths and

TABLE 2

COMPARISON OF SURGICAL RESULTS IN COARCTATION OF AORTA AND CARCINOMA OF STOMACH

	OPERATIVE MORTALITY *(per cent)*	5-YEAR SURVIVAL IN PATIENTS SURVIVING OPERATION *(per cent)*
Coarctation of aorta	5	100*
Carcinoma of stomach	8	32

*Hypertension absent in 92 per cent.

TABLE 3

ABDOMINAL AORTIC ANEURYSMS: INTERVAL BETWEEN DEATH AND TIME OF DIAGNOSIS*

PERIOD *(years)*	PER CENT OF TRACED PATIENTS DEAD AT END OF INDICATED PERIOD
1	33
2	42
3	51
5	81

*Modified from Estes.

no complications from the operation. It is too early as yet to judge the long-term results of this procedure. It is fair to state, however, that this technic, although tedious and at times difficult, can be done with relative safety, and it gives promise of being a highly efficacious operation.

Mitral stenosis—The operation for mitral stenosis is an intracardiac procedure that has been done often enough to allow certain conclusions as to its value. My colleagues and I are of the opinion that all patients who have mitral stenosis and who have significant symptoms should be considered candidates for mitral commissurotomy.

The results of this operation to date have been excellent. In my own series, now numbering 105 cases, the operative mortality rate has been 8 per cent. Approximately 90 per cent of the patients surviving operation have obtained significant improvement, and many of them are now virtually asymptomatic. The medical profession should acknowledge its debt to Bailey and his associates[16] and to Harken and his co-workers[17] for their leading efforts in the treatment of this serious disease.

Atrial septal defect—Another intracardiac operation that recently has been established as being of proved efficacy is the closure of atrial septal defects. These defects are sometimes small, in which case surgical treatment is not required. When the defects are large, 70 to 90 per cent of the blood returning to the left atrium from the lungs is shunted across the septal defect into the right atrium to go back to the right ventricle and again through the pulmonary circuit. This action imposes a tremendous load on the right ven-

tricle, which eventually fails. Even before this occurs, patients who have atrial septal defects are handicapped by fatigue and breathlessness and, occasionally, by stunted growth.

Although no unanimity of opinion exists among surgeons engaged in cardiovascular work as to the method of surgical approach to these lesions, it is generally agreed that closure of atrial septal defects can be performed with considerable safety.[18-21] The various methods that have been utilized will not be reviewed, but I shall outline the experience at the Mayo Clinic. Operations have been done on five patients who had atrial septal defects; no deaths have occurred. Only partial closure was obtained in the first patient, but completely satisfactory closures were accomplished in the last four patients. The atrial well devised by Gross has been used to provide an entrance into the right atrium, and the defect has been closed by sewing a piece of polyvinyl plastic sponge in place.[22]

This may not be the ultimate method of closure, but I have found it safe and satisfactory. Complete closure of these large atrial septal defects gives to such patients a normal life expectancy, whereas prior to such repair the existence of the large left-to-right shunt through the defect posed a serious threat to continued existence.

Anomalous pulmonary venous connection—On occasions, a physiologic abnormality similar to that existing in patients who have atrial septal defects is produced by anomalous connections of the veins draining one or both lungs (figure 1). In such situations, already oxygenated blood is shunted back into the right atrium whence it again must pass through the right ventricle and the pulmonary circuit. Strain on the right side of the heart results, and these patients suffer from breathlessness, fatigue and ultimately right heart failure. On occasions, this anatomic abnormality can be completely corrected by a properly planned surgical procedure.[23]

Recently, my associates and I cared for a young man who had increasing breathlessness and fatigue. Precise study in the cardiovascular laboratory by Dr. Wood and his group demonstrated a large left-to-right shunt. Further study made it certain that this resulted from anomalous connection of the veins draining the entire left lung. We became convinced

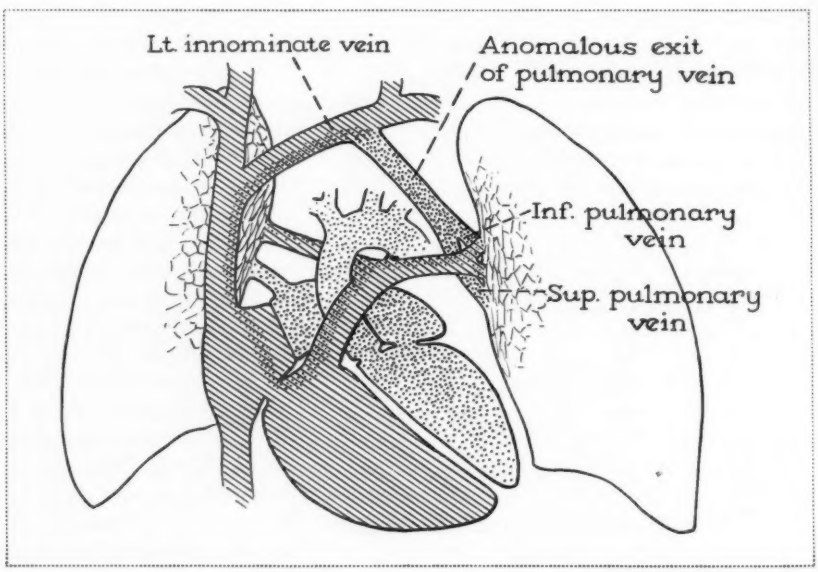

FIGURE 1. Anomalous pulmonary venous connection of the left lung to the left innominate vein, causing pulmonary recirculation. Note that veins of the right lung drain in a normal fashion into the left atrium.

Reproduced from Kirklin, J. W.: Surgical treatment of anomalous pulmonary venous connection (Partial anomalous pulmonary venous drainage). Proc. Staff Meet., Mayo Clin. 28:476-479 (August 26) 1953.

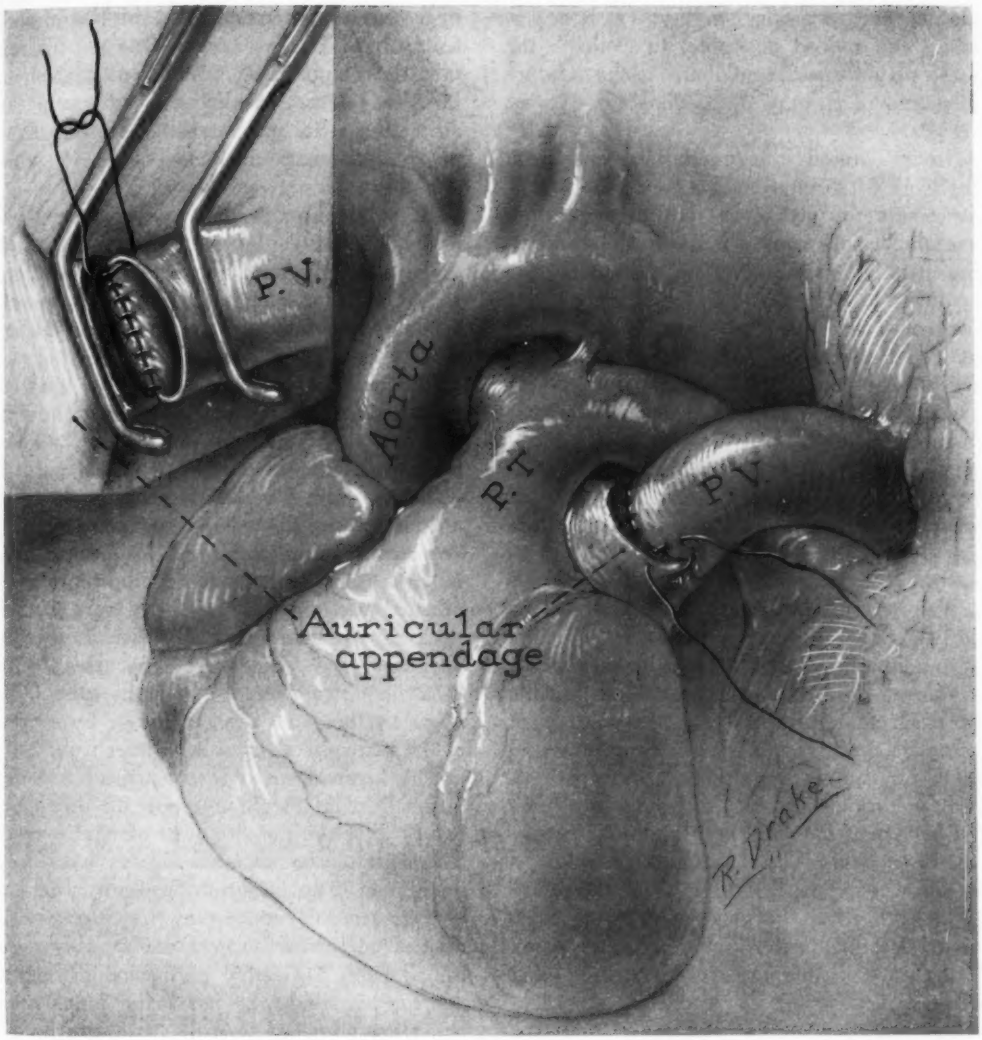

FIGURE 2. Surgical correction of anomalous pulmonary venous connection. The pulmonary vein draining the left lung has been disconnected from the left innominate vein and is shown being sutured to the left atrium. The inset in the left upper portion shows the location of the first line of sutures.

Reproduced from Kirklin, J. W.: Surgical treatment of anomalous pulmonary venous connection (Partial anomalous pulmonary venous drainage). Proc. Staff Meet., Mayo Clin. 28:476-479 (August 26) 1953.

that this serious abnormality could be corrected by operation, and this proved to be the case (figure 2).

Such anomalous pulmonary venous connections pose a serious threat to the future well-being of the afflicted patient. This operation changed an abnormal situation to a normal one and has given to this patient a normal life expectancy.

Future Potentialities of Cardiovascular Surgery

It is manifestly impossible to predict the future of any field of human endeavor, in-

cluding cardiovascular surgery. Yet it is possible, and indeed desirable, to evaluate the factors that must contribute to any future advances in surgery of the heart and great vessels.

In my opinion, four foundation stones form the basis for future development. The first is awareness of physicians that many cardiovascular lesions can be treated safely and efficiently by operation. The second is the acquisition of ever more precise methods of diagnosis. The third is the evolution of new and special surgical technics. The fourth is the development of well-integrated teams for executing the required surgical procedures.

In cardiovascular disease, as in disease of all types, the general physician in small or large communities is the backbone of the various echelons of medical care. Patients are usually first seen by these general practitioners, and it is incumbent on them to recognize serious cardiovascular disease in its earliest stage, preferably while it is relatively asymptomatic so that the condition may be evaluated promptly with regard to possible surgical intervention. Further, physicians must be aware of the results of such operations and their advantages and pitfalls, for patients rightly lean heavily on the family physician for guidance in deciding for or against an operation advised by a specialist.

The second foundation on which the future is to be built is the acquisition of methods of precise diagnosis. It was sufficient in the past to make a diagnosis of rheumatic heart disease. Today, this is an incomplete diagnosis. Instead, careful assessment of the status of the mitral, tricuspid, aortic and pulmonic valves must be made in every patient who has rheumatic heart disease. Even this is not enough. The condition at the mitral valve, as an example, must be further pinpointed as to whether it is pure mitral stenosis, mitral stenosis plus mitral regurgitation or free mitral regurgitation without mitral stenosis. Again, it is no longer sufficient to make a diagnosis of probable tetralogy of Fallot. Instead, the decision must be made as to the precise nature of the congenital pulmonic obstruction, whether it is at the pulmonic valve or a few millimeters below, in the outflow tract of the right ventricle. One must ascertain the nature of the venous-arterial shunt in such a case, localizing it accurately to either the atrial or ventricular septum. Even finer distinctions must be made in other situations.

As surgical procedures are further amplified, the need for absolute accuracy in the diagnosis of the most complex malformations and diseases of the heart and great vessels becomes essential. Such precise diagnoses are made by careful clinical study of the patient, with intelligent interpretation of the history, physical findings and roentgenologic studies. Angiocardiography must be employed in certain situations. In many instances, cardiac catheterization done by an experienced team utilizing complex technics of unquestioned accuracy must be employed. It is regrettable but true that such studies demand more complicated methods rather than more simple ones as the field of cardiovascular surgery advances. It is, of course, also true that a B-52 jet Stratofortress bomber cannot be flown by the same instruments or by a crew of the same size utilized in a Piper Cub.

The formulation of new surgical technics is the third of the foundations on which depend the future potentialities of cardiovascular surgery. Some technics already have been mentioned. The important work by Bigelow and associates[24] concerning hypothermia in relation to cardiac surgery can be only mentioned here. Perfection of mechanical methods for bypassing the heart and lungs soon will allow surgeons to work at leisure in the human heart in a bloodless field, in my opinion. Some are critical of efforts in the direction of perfecting such bypasses, considering that they are too cumbersome ever to be applicable with safety to patients. I think this is analogous to flying an airplane through the sonic barrier. Until such flight actually had been done, one could theorize that it might not be possible, but the moment the feat was accomplished, it was obvious that it was indeed possible. Gibbon[25] successfully bypassed the heart and lungs of a young woman for 30 minutes by means of a mechanical apparatus

while an intracardiac operation was performed. The patient survived and is alive and well today. Therefore, bypassing can be done, and it remains only to perfect these technics until they become completely safe.

Finally, the coordination of a group of highly specialized persons into a team is essential to the future of cardiovascular surgery. Fortunately, or perhaps unfortunately, the day has passed when the surgeon can be a prima donna, demanding for himself the spotlight and the slavish obedience of all around him. He remains, of course, a key figure in this field but only as a member of a team that includes the pediatrician, the cardiologist, the roentgenologist, the anesthesiologist and the physiologist in the cardiovascular laboratory. It is only the synchronized efforts of this group that allow modern cardiovascular surgical procedures to be done safely and accurately. It is only by such cooperation of all concerned that hope and assistance can be offered to patients who place their lives in the hands of such a group.

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AUTHOR'S CORRECTION

In the abstract preceding the article, "Diseases of Lymph Nodes," by Dr. Ovid O. Meyer (February 1954, p. 128), the last two sentences should have read: "The patients should be treated when symptoms are present, and, when they are asymptomatic, normal activity is permissible."

Office Diagnosis of Pheochromocytoma

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The hypertension of pheochromocytoma is often characterized by distinctive signs and symptoms. These clinical manifestations and the recent introduction of simple pharmacologic tests make the office diagnosis of even the "silent" pheochromocytoma feasible. Early diagnosis and surgery are mandatory if cardiovascular damage or malignant changes are to be prevented.

ALFRED SOFFER

THE first line of defense against the ravages of pheochromocytoma is the office examination. Increasing awareness of the urgency of early diagnosis of pheochromocytoma promises a dramatic reduction in the annual 800 deaths resulting from the disease. The introduction of simple pharmacologic tests and the recognition that pheochromocytoma is more often associated with sustained than with paroxysmal hypertension has enabled the practitioner to diagnose hypertension secondary to pheochromocytoma long before that hypertension has produced irreversible blood vessel changes.

Pheochromocytoma is occasionally malignant (less than 10 per cent of all cases[1]); yet it ordinarily does not kill by invasion. Instead, pheochromocytoma may be thought of as "the goiter of the abdomen." Just as hyperthyroidism produces effects on distant organs by the elaboration of a blood-borne hormone, so does pheochromocytoma influence distant cells by releasing excessive amounts of readily recognizable hormones into the circulation. Epinephrine and norepinephrine are the two endocrine products secreted by pheochromocytoma which explain all the signs and symptoms associated with this chromaffin tumor. The diagnosis of pheochromocytoma is achieved by three methods of investigation: (1) clinical evaluation, (2) pharmacologic tests and (3) roentgen studies.

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Clinical Evaluation

When significant quantities of epinephrine are being released into the blood, three major clinical clues occur which should make the physician think of pheochromocytoma: (1) the presence of symptoms, either sustained or paroxysmal, suggesting hyperepinephrinemia, (2) hypertension associated with hypermetabolism, and (3) hypertension associated with diabetes mellitus.

Paroxysmal attacks—When paroxysmal attacks of hyperepinephrinemia occur, the patient will describe episodes of palpitation, epigastric discomfort, pounding headaches,

marked apprehension and nausea. If observed during an attack, the patient will evidence pallor and cold extremities.

Smithwick's criteria—Dr. Reginald Smithwick,[2] in a superb analysis of the clinical characteristics of pheochromocytoma, pointed out that the patient with pheochromocytoma manifests excessive sweating due to stimulation of central parasympathetic centers. He noted also the coexistence of typical epinephrine effects on peripheral vessels with resultant coldness, blanching, mottled discoloration and tingling of hands and feet. Finally, Dr. Smithwick observed that, unlike essential hypertension, pheochromocytoma causes postural hypotension and postural tachycardia.

Metabolic effects—In the presence of hyperepinephrinemia the patient's metabolism will be elevated as evidenced by an abnormally high basal metabolic rate and a continued low-grade temperature elevation. The radioactive iodine uptake in these instances is, of course, normal and antithyroid medication is futile. This phenomenon is explained by the fact that epinephrine is the only hormone other than thyroxin which directly affects the cellular metabolic rate.

Diabetic picture—Epinephrine is notoriously diabetogenic and therefore pheochromocytoma may be unmasked if suspicion is directed toward hypertensive patients who manifest glycosuria, hyperglycemia or a diabetic glucose tolerance curve.

Norepinephrine versus epinephrine—A fortunate union of pharmacologists and clinicians recently unraveled the mystery of the "silent pheochromocytoma."[3] From their combined efforts, we have learned that epinephrine is responsible for the metabolic and central cardiac effects. Epinephrine, however, does not ordinarily produce diastolic hypertension, and the moderate systolic blood pressure rise (to 180 mg. of mercury) is due to an associated increased cardiac output. It is the norepinephrine component of pheochromocytoma's secretion which produces the asymptomatic paroxysmal or persistent arteriolar vasoconstriction. The resultant systolic and diastolic hypertension characteristically demonstrates a negative cold pressor test response which may help to distinguish it from essential hypertension. It should be stressed that in some cases of pheochromocytoma norepinephrine produces not only hypertension but also the metabolic changes. This is because in larger amounts norepinephrine resembles epinephrine in its action on metabolism and cardiac musculature.

Other clinical clues—Two other clinical clues may now be added to this list. Recurrent attacks of acute nephritis are suggestive, and Fertig and associates[4] have discovered pheochromocytoma to be the inciting factor in a case which they labeled "paroxysmal nephropathy." Glushien, Mansuy and Littman[5] stressed that neurocutaneous diseases may frequently be associated with pheochromocytoma. They urged the clinician to look for cutaneous, ocular, osseous, neurologic and developmental abnormalities in hypertensive patients. They also stated that neurofibromas of intercostal nerves may produce notching of ribs, and if, "In a patient with hypertension and notched ribs no other evidence of coarctation of the aorta is found, pheochromocytoma should be suspected." One word of caution: The presence of one or more of these clinical clues must be interpreted not as a definitive diagnosis but rather as an indication for further investigation. Hypertension will be associated with true diabetes mellitus more frequently than with pheochromocytoma, just as true hyperthyroidism and essential hypertension may occur concurrently. Paroxysmal hypertension moreover may appear with nephritis, aortitis, hyperthyroidism, tabes dorsalis and central nervous system injury,[6] and diencephalic stimulation[2] in the course of essential hypertension.

Pharmacologic Tests

The provocative pharmacologic tests (histamine, ETAMON® chloride and MECHOLYL®) which produce paroxysms of hypertension in patients with pheochromocytoma are best performed in a clinic or hospital environment because of the high incidence of side effects. More commonly, however, pheochromocytoma produces sustained hypertension. Therefore, it is particularly fortunate that a simple pharma-

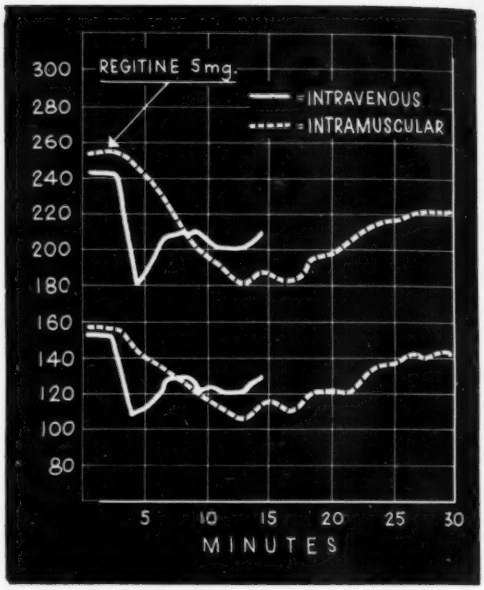
cologic test, using REGITINE®, which is diagnostic in the presence of sustained hypertension due to pheochromocytoma, is also readily applicable for office use. Since hypertension secondary to norepinephrine may be relatively asymptomatic, a screening test such as Regitine is needed in most hypertensive patients.[7]

Action—Regitine (C7337) blocks the pressor effect of epinephrine and norepinephrine (adrenolytic effect), although the latter is twice as resistant to this inhibition. In larger amounts, Regitine blocks sympathetic nerve impulses (sympatholytic effect) which explains its beneficial effects in essential hypertension[8] and peripheral vascular disease.[9]

Administration—Regitine may be given intravenously or intramuscularly. The patient rests until a stabilized blood pressure is obtained as a base line. Regitine may be injected rapidly, following which blood pressure readings are made every 30 seconds for three minutes and then every minute for seven minutes (or longer if the blood pressure is still changing significantly). After the intramuscular use of Regitine, blood pressure readings are made every five minutes for one-half hour. Following the use of Regitine, no serious untoward side effects have been reported.

A positive test—The Regitine test should be performed only if the systolic blood pressure is above 170 mm. and the diastolic pressure above 110 mm. If the blood pressure is only slightly elevated, it is probable that circulating epinephrine or norepinephrine are at low levels, at least temporarily. Under the latter conditions, only a slight blood pressure drop may bring the levels within normotensive range and make interpretation difficult. Over one-half of all hypertensive patients will have a minimal blood pressure drop after Regitine administration. We, therefore, use the criteria established by Gifford and associates,[10] that a Regitine test may be called positive only if the blood pressure fall is more than 30 mm. systolic and 20 mm. diastolic. A comparison of positive responses to intramuscular and intravenous Regitine is presented in accompanying figure.

False positive tests—Sedatives, narcotics or anesthetic agents given within 24 hours before a Regitine test may produce false positive results. Thiocyanates should not be administered for four to six days preceding Regitine for this same reason. If the Regitine test (or piperoxan[11]) is performed in the presence of the uremia, a significant blood pressure drop may occur in the absence of pheochromocytoma. It must be stressed that even if the test conditions are rigidly supervised, intravenous Regitine frequently produces false positive results (as high as 20 per cent of all cases, according to a personal communication from Dr. Mark Nickerson).



Typical blood pressure responses to the intravenous and intramuscular Regitine test in the presence of pheochromocytoma.

False negative tests—Standard doses of Regitine block only quantitatively predictable amounts of pressor substances. This means that larger amounts of circulating epinephrine or norepinephrine can break through the adrenolytic drug inhibition. If the patient is tested during periods when the pheochromocytoma is emitting larger amounts of pressor hormones, false negative tests may result. Such false results have been recorded following Regitine testing by the intramuscular route. False negative tests following the use

of intravenous Regitine have not yet appeared, but we can expect them to occur.

Piperoxan—Under proper test conditions, piperoxan (BENODAINE® hydrochloride) is the only adrenolytic drug which almost never produces false positive reactions. It should, therefore, be used as a confirmatory test in every case which demonstrates a positive Regitine test. Because of the relatively high incidence of side reactions, it is not ideally suited for an office test. For the alarming pressor reactions which may occur in the absence of pheochromocytoma, amyl nitrite pearls should be available as an antidote. Blood pressure changes of great magnitude are dangerous in hypertensive patients, because their cardiovascular reserve is usually impaired.[12]

No perfect test—In suspected cases of pheochromocytoma, a battery of pharmacologic tests often must be employed since there is, at this time, no single foolproof pharmacologic test for pheochromocytoma.

Roentgen Studies

Flat plates of the abdomen and intravenous pyelography are invaluable not only in the diagnosis of chromaffin tumors (pheochromocytoma) but also in aiding the surgeon to localize such masses. Rarely, a thoracic chromaffinoma may be visualized in a chest roentgenogram. Unfortunately, roentgenography proves of assistance in the diagnosis of pheochromocytoma in only a minority of cases.

Summary

Pheochromocytoma is responsible for 800 of the 175,000 annual deaths due to hypertension. Moreover, every pheochromocytoma must be regarded as potientially malignant. Therefore, in the office examination, there is a double responsibility and an urgent need to diagnose this completely curable disease early. The alarm is sounded early in many cases, for the intermittent discharge of epinephrine secreted by some pheochromocytomas produces readily recognizable paroxysms of palpitation, headaches and apprehension. Even without paroxysms, hyperepinephrinemia produces hypermetabolism in the presence of a normal radioactive iodine uptake. Epinephrine is diabetogenic, and in many instances the blood and urine studies suggest diabetes mellitus. Pheochromocytoma may produce a picture of paroxysmal nephritis. A more recent clinical clue has been the description of the frequent association of neurocutaneous diseases with pheochromocytoma. The norepinephrine component of pheochromocytoma's secretion is responsible for the systolic and diastolic hypertension which may be paroxysmal or malignant, but most often is sustained. Since such hypertension is often asymptomatic, pharmacologic tests are obligatory in unmasking the true etiology. Regitine is readily applicable for office use, and it serves admirably as a screening procedure. After a positive Regitine test and in other suspected cases, the patient must be studied in a hospital environment. Confirmatory pharmacologic tests must be performed, since at this time there is no single foolproof test available for the diagnosis of pheochromocytoma.

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DIAGNOSTIC CLINIC

Indeterminate Pulmonary Lesions

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Indeterminate pulmonary lesions may include those caused by (1) tumors, (2) inflammatory conditions which are either tuberculous or nontuberculous and (3) congenital abnormalities. These lesions are defined as indeterminate when all methods of diagnosis short of exploration fail to identify them. Since 20 to 40 per cent of all patients with primary carcinoma of the lung are in this group, it is very important to make an exploration and biopsy in order to institute adequate surgical therapy.

INDETERMINATE pulmonary lesion" (from the clinical point of view) means any pulmonary lesion which resists recognition or identification, short of exploratory thoracotomy and biopsy. The main conditions which fall into this classification may be divided into three groups: (1) neoplastic lesions, either primary or metastatic, (2) inflammatory lesions, either tuberculous or nontuberculous, and (3) congenital abnormalities, which may be either vascular or pulmonary.

Since early recognition is perhaps more essential in malignant disease than in the other two groups (although, as I shall bring out later, many lives will be saved if these lesions are recognized in the other groups also), I should like to refer to the present status of our thinking about malignant tumors of the lung. In the early stage of primary carcinomas of the lung, about 20 to 40 per cent are unidentifiable without biopsy, in spite of our ever-increasing diagnostic methods. In my experience (and we all have different experiences according to the cases we treat), between 15 and 20 per cent of these indeterminate pulmonary lesions have been malignant. Don't confuse what I am talking about with the so-called coin lesions; they may be included in this group, but the group is not confined to the coin lesion. As I have said, about 20 to 40 per cent of early malignant tumors, metastatic or primary, cannot be diagnosed without thoracotomy and biopsy. The cytologic test for identifying these tumors has helped a great deal, but in the early stages of development only approximately 10 per cent will give a positive test.

Indeterminate pulmonary lesions may be

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silent; in this group, the malignant, tuberculous and congenital lesions occur perhaps in that order of incidence, although that will vary somewhat. Another group will present only the picture of hemoptysis, and the patients will be perfectly well except for occasional hemoptysis; in this group, we put congenital lesions first, malignant second, and tuberculous third. In the case of pulmonary suppuration caused by indeterminate pulmonary lesions, the order of incidence is congenital lesions, neoplasms and foreign bodies (obstruction of bronchus).

What means do we have of identifying these lesions? There are the history and physical findings, but, as I mentioned earlier, all too frequently there is no history to guide us and the physical findings may be entirely normal.

In addition to a history of symptoms, however, we note the age, sex, geographic location of residence of the patient, and any other factors which may be important in correlating other findings with this information. The patient's occupation may offer a lead to the cause of the lesion.

There are also sputum studies both for acid-fast organisms and for malignant cells. If the sputum is examined carefully and properly, it frequently is more helpful than a bronchial aspirate obtained through a bronchoscope.

X-rays and fluoroscopy are, of course, important and give us a great deal of information. Fluoroscopy frequently shows a relationship to other organs or other structures that is not brought out by an x-ray. X-rays may be regular posterior-anterior and lateral views, but often a planogram will bring out information not obtained from regular films. In some patients a bronchogram will help a great deal to identify the lesions.

Our routine includes three skin tests on all our patients: tuberculin, histoplasmin and coccidioidin. These patients may not live in the regions where histoplasmosis and coccidioidomycosis usually occur, but, surprisingly they may have lesions of those diseases.

Bronchoscopy, unfortunately, does not help us much in most of these cases other than to furnish bronchial secretions for study.

Lymph node biopsy may be of real value where possible metastases have occurred.

Diagnostic pneumothorax and diagnostic pneumoperitoneum at times will bring out valuable information.

With that introduction, I should like to describe a number of patients who, for one reason or another, presented problems which could not be diagnosed without exploratory thoracotomy.

The first patient was a 41 year old man who came in after being rejected for military service. The rejection was based on the presence of a lesion in his lower right lung and was somewhat smaller two months before he reported to us. Examination showed nothing other than the "spot" on the x-ray of the chest. The patient decided to have nothing done about it. A few months later, the spot had increased in size.

That brings up the question of whether we should "wait and see" what an x-ray made two or three months later will show. In most cases this attitude is completely outmoded as a method of diagnosis. Frequently the size of the shadow will change very slowly, as happened in this case. At one time, in a period of about 14 or 15 months, a cavernous area or a "spare" area was seen in the center of the opacity. If the patient had been seen at that time, the diagnosis might have been tuberculosis, although the affected area was in a part of the lung not frequently involved by tuberculosis.

Surgical exploration was done at the end of this time, the delay being due mostly to the patient's not being able to agree to an operation.

Squamous cell (primary) carcinoma of the lung was found, with some necrosis in the center, explaining the cavity seen in his x-ray.

The next patient was a 45 year old man who gave a history of cough, low grade fever, and some bleeding from the lung. In a man of his age with those symptoms, we would have to suspect carcinoma as the most likely cause of the x-ray appearance of his chest. A planogram showed what appeared to be cavity formation (figure 1). A cavity, we know, does not rule out a diagnosis of carcinoma; it could be either a tuberculous or a nontuberculous

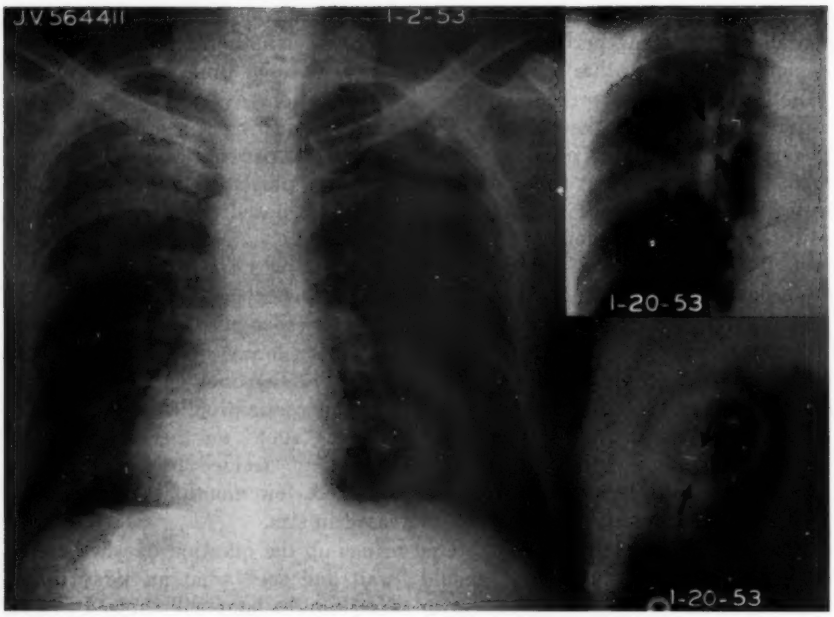

FIGURE 1. Planogram of 45 year old man showing cavity formation.

lesion, or it could be a cavitary carcinoma. This also could have been a congenital pulmonary type of malformation of the lung with superimposed infection.

It was not until the patient was operated, and the surgical specimen was found to be a nontuberculous lung abscess without evidence of carcinoma, that a definite diagnosis was possible.

Another patient was a man, 64 years of age, whose first symptoms were present for only a short time before he entered the hospital. A roentgenogram made approximately a year and eight months earlier was normal. On admission an x-ray revealed a cavitary lesion in the lower part of the left lung. This man had had symptoms suggesting pneumonia. However, when his fever went down the x-ray appearance persisted, so that a diagnosis of lung abscess was made before he was sent into the hospital. After examination in the clinic, no definite evidence for a specific diagnosis could be obtained, although it was thought that there was congenital cystic malformation of the lung with superimposed infection. We changed the diagnosis from lung abscess to an infected cyst because his symptoms had, for the most part, disappeared.

We were quite surprised when we found that the lesion was a cavitary carcinoma, lined throughout by a squamous cell type of tumor.

The earlier x-ray had also indicated some change in the upper outer portion of the right lung, so that when the carcinoma was found, it was thought that the patient was in no shape for a second operation. He was followed for a few months, the shadow in the right lung becoming larger. He appeared to be much better, he was stronger and, in spite of his age of 64 (he had had only a lobectomy on the left side), it was thought that he might be able to have the tumor removed. On exploration, two tumors were found, one in the upper lobe and one in the superior segment of the lower lobe. Those areas were removed by an upper lobectomy and by a superior segmentalectomy of the right lower lobe. The microscopic appearance of the right upper lobe tumor was that of a squamous cell carcinoma. In other words, this patient had three

separate carcinomas, unless the two on the right side represented a spread from the cavitary tumor on the left side. That, of course, is impossible to rule out.

The next patient was a 60 year old woman. I mention the sex particularly, because we know that carcinoma of the lung of the primary type is much less frequent in women than in men, perhaps 1 in women to 10 or 12 in men, although that ratio may be changing somewhat at the present time. This patient was entirely asymptomatic when she was first seen. At one time she had had a cough which was indefinite and which had cleared spontaneously. An x-ray taken in 1946 demonstrated a shadow in the mid-right lung field.

I saw the patient for the first time in 1949. A lateral view made then showed that the shadow had become somewhat larger in the three years since she was first examined. All efforts to make a definite diagnosis failed. At operation the lesion was found in the middle lobe. A microscopic section showed it to be an adenocarcinoma. Although no gross metastases were found, adequate surgical therapy was delayed three years by the "wait and see" attitude.

One usually thinks of malignant tumors of the lung as growing more rapidly than some of these I have described, especially the adenocarcinoma. However we have followed these tumors with x-rays made one place or another for periods of three to four years, some proving to be adenocarcinomas.

The next patient was another women, 42 years of age. Her only symptom had been hemoptysis. An x-ray made about two years earlier showed nothing abnormal. About a year ago, we saw a fairly circumscribed shadow in the upper part of the left lung near the mediastinum, with some calcification (figure 2). In retrospect, of course, this calcification probably explains the bleeding and brings out the diagnosis. At the time she was seen, it was felt that she had one of the following: (1) a benign tumor of the type seen more commonly in women than in men, but also appearing frequently in the young age groups—as early as 30 or before—as well as in the years beyond; (2) possibly something like a hamartoma, which is a congenital lesion; (3) or some obscure type of inflammatory lesion, possibly tuberculous, although tuberculin tests were normal. Surgical exploration was necessary for a definite diagnosis.

X-ray studies made after an upper lobectomy showed a calcified lymph node which had eroded into the bronchus, thus forming a broncholith. This was beyond the view of the bronchoscope, even a telescopic bronchoscope. It had produced obstruction, with infection and atelectasis, which was responsible for the shadow. The broncholith itself was a calcified lymph node.

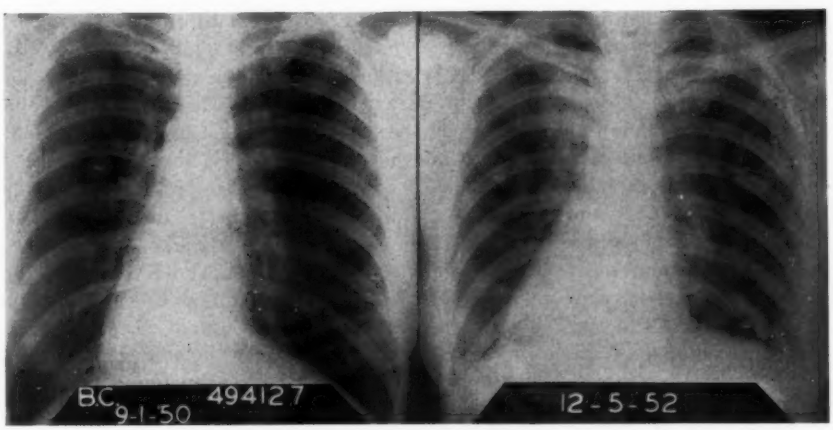

FIGURE 2. X-ray showing a circumscribed shadow in the upper part of the left lung near the mediastinum, with some calcification. Patient was a 42 year old woman.

The next patient was a 28 year old student, again with one symptom, namely, bleeding. X-rays made approximately three months apart showed little change in the circumscribed opacity. A picture made two years previously was said to be entirely normal. It had been lost, but as it was taken in a reputable institution we will assume that it was normal, since it was so reported.

In a man of 28 whose occupation and location of residence gave us no help, we would most likely think of either a congenital lesion or possibly a hamartoma. I have seen hamartomas grow to considerable size when they had not been seen at all two or three years earlier.

The possibility of a cyst should be considered, and by that I mean an interlobar type of cyst or fluid-filled pulmonary cyst.

The patient did not have one test which would have brought out the diagnosis, that is, an angiogram. We made a diagnosis of this type of lesion (atrioventricular fistula) in another patient by injecting DIODRAST® and showing the vascular communications with the lesion. However, in this case it would have been much less easy to demonstrate, because it turned out to be an aneurysm and was approximately two-thirds obstructed by an organizing thrombus. The aneurysmal sac and communicating branches could be seen in the injected specimen. A microscopic section showed only about a fourth of the aneurysm filled with circulating blood, the rest being an organizing thrombus. When these aneurysms have large communicating branches, there are marked changes in the patients' blood pictures; they have clubbing of the fingers and a marked decrease in arterial blood oxygen saturation. It is not difficult to diagnose these lesions before exploration when changes in the blood are present.

Another patient was a 48 year old woman who was entirely asymptomatic. She was followed from 1949 to 1952, her x-rays showing a persistent opacity in the upper right lung field, 1.0 cm. in diameter. There was so little change in the size of the lesion that her doctor felt it was "innocuous" and would cause no trouble. It is impossible to make a pathologic diagnosis of a lesion like this from the x-ray alone. In this patient we had one lead. She had had a radical mastectomy for carcinoma of the breast 14 years earlier. In our experience it is not usual to find a single metastasis from carcinoma of the breast to the lung, but that is what this turned out to be—an adenocarcinoma. Whether it was a primary or metastatic lesion was impossible for the pathologist to say. We have removed an adenocarcinoma of a similar size from a second patient who had had a breast carcinoma removed 12 years earlier. Both patients are free of evidence of tumor one and two years later.

The next patient was a 16 year old girl whose only symptom was cough. An x-ray showed a shadow in the left hilum and calcification in one area. All of her tests, including a tuberculin test, were normal. We have seen one or two patients with what were found to be tuberculous lesions who had negative tuberculin skin tests.

This patient's bronchogram showed no filling of what would be the middle lobe on the right side, i.e., the lingular area of the left upper lobe. She was found to have what is called a "middle lobe syndrome"; it is simply an obstructive type of nonspecific pneumonitis, usually due to enlarged glands.

In young women of this age (16 years) there are one or two other conditions to consider in differential diagnosis. Histoplasmosis is one; the other is congenital malformation of the lung.

The next patient was a 25 year old woman doctor who had just finished her internship and had been perfectly well. An old x-ray of her chest showed nothing abnormal. A routine x-ray was made at the end of her internship (figures 3a, b and c). She had no symptoms and results of all tests made were normal. The Kveim test for sarcoidosis was not made since she chose not to wait the six weeks usually necessary for that test. During surgical exploration, a number of enlarged glands were found in the hilum. Removal of one of those glands showed definite evidence of sarcoidosis in the anterior part of the hilum, as indicated in a lateral view taken in

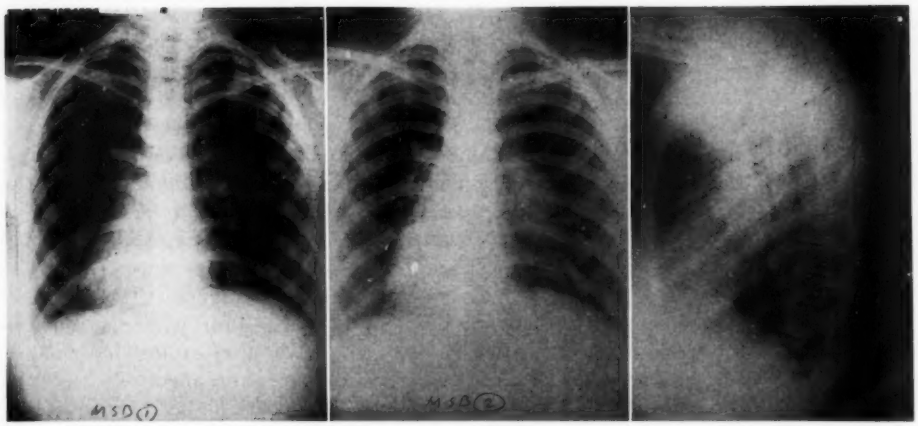

FIGURE 3. Routine x-ray studies of 25 year old woman, showing nothing abnormal. Patient was later found to have sarcoidosis.

1951. These glands have subsequently entirely disappeared and, at the present time, the patient's x-ray appears normal. We are gradually learning more about this lesion by the study of various stages of the disease.

The next patient was a 60 year old white man whose complaint was cough and hemoptysis. He was followed for about a month but no definite diagnosis could be made (figure 4). We then did a lobectomy, and, on examination of the surgical specimen, we saw a very interesting type of tumor, a primary malignant tumor of the lung, which has been called by various names, the best of which is probably bronchiolar carcinoma. It is sometimes called alveolar cell carcinoma. It also presented evidence of vascular malformation, and in years to come we may find some definite connection between the vascular type of malformation, or even the pulmonary type, and some of these malignant tumors.

The important fact about this tumor is that

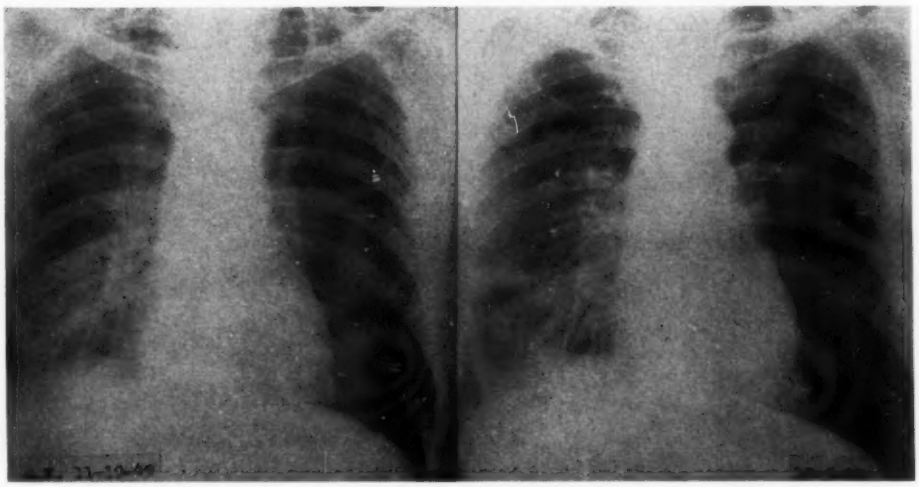

FIGURE 4. X-ray of 60 year old man; a primary malignant tumor of the lungs was found during surgery.

formerly it was called adenomatosis and was usually seen bilaterally. We feel now, from information more recently obtained, that it arises in one location, subsequently spreads throughout both lungs and, in that way, becomes inoperable. A number of these tumors have been resected while they were in one location, but only within the last few years. They have not been followed long enough to know whether more lesions will arise in other locations.

A 57 year old man seemed to have one of the so-called "coin lesions," although it did not look like a coin lesion on the x-ray. When the heart was rotated out of the way, it was found that the lesion was not in the bronchus; it was in the pulmonary tissue and quite well circumscribed (figure 5). The patient was entirely asymptomatic.

Microscopic examination showed that it was a hamartoma, a cartilaginous tumor in this case. This type of tumor is really a congenital lesion, although it is classified at times as a tumor.

In another case, a 46 year old Negro was followed for a number of years for bilateral emphysema. He came in for a routine x-ray and a lesion was found in the lower left lung field (figure 6). This man had no symptoms whatever and all tests were normal. Surgical exploration was necessary in order to make a diagnosis. The diagnosis was an early stage of squamous cell carcinoma.

The more such cases one sees, the less sure one is of what they are apt to be. Unless the patient is in otherwise poor physical condition or has poor pulmonary or cardiac reserve, the *risk of exploration will be less than the risk of not operating* and of taking a chance on the absence of a serious lesion.

The last patient to be discussed was a young girl of 17 who had had some cough but no other symptom. A circumscribed opacity on an x-ray showed her lesion. Results of all tests were negative, but one was not made and it probably would have given a positive result, i.e., a histoplasmin skin test. A mass of calcified tissue was found which was originally a gland between the upper and the lower lobes, involving the lower lobe. This mass was re-

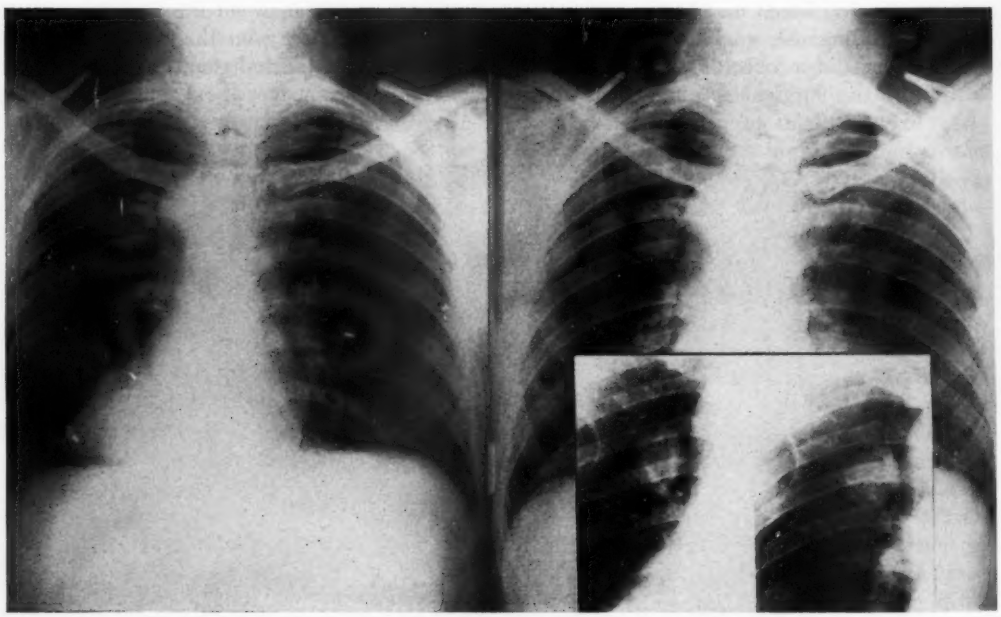

FIGURE 5. X-ray study of this patient disclosed what appeared to be a coin lesion. When the heart was rotated out of the way, a well-circumscribed lesion was found in the pulmonary tissue.

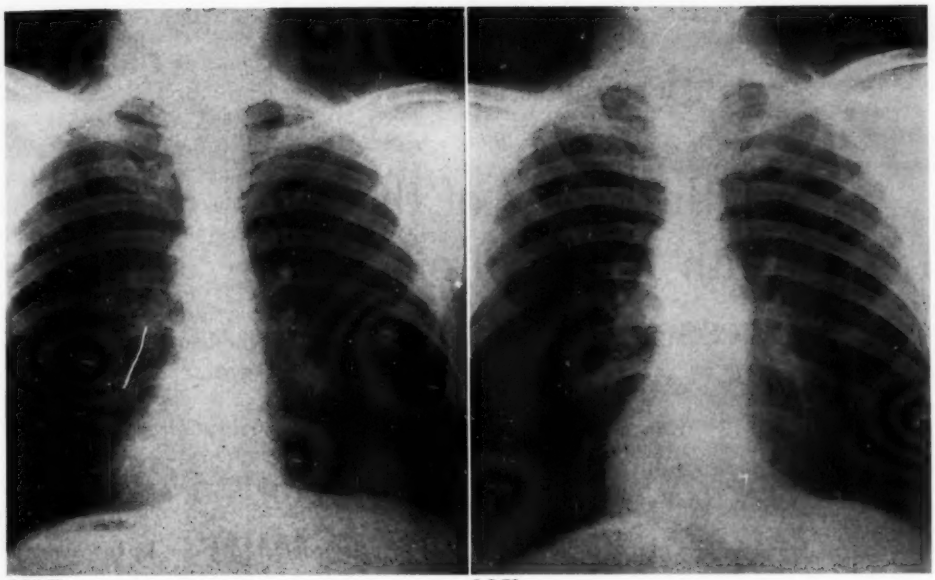

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FIGURE 6. Routine x-ray of 46 year old man disclosed lesion in the lower left lung field.

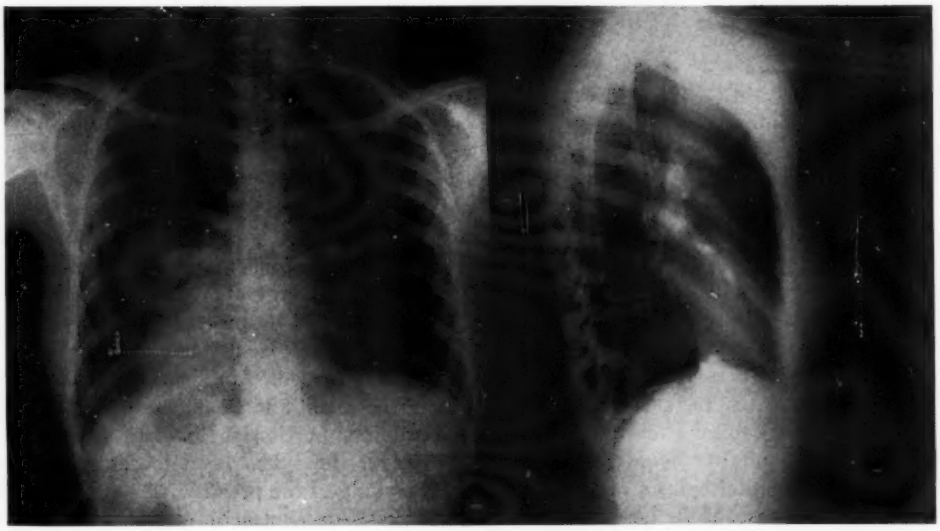

FIGURE 7. Circumscribed opacity on x-ray of 17 year old girl indicated presence of lesion.

moved. No definite diagnosis was made, even after the lesion had been removed. (Figure 7.)

I have tried to indicate with these illustrative cases how difficult and how impossible it is to make a definite diagnosis in cases presenting these indeterminate pulmonary lesions. If the patient's condition permits, after all tests have been used to establish a diagnosis, surgical exploration is justified and will save many lives.

Arthroplasty of the Hip with Removal of Lesser Trochanter

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Arthroplasty of the hip with removal of the lesser trochanter gives the disabled patient a usable, painless and comfortable hip. This procedure has been used over 20 years and has withstood the test of time. Patients over 70 years of age with subcapital fractures of the neck of the femur are ideal candidates for the procedure, as it is a recognized fact that poor results usually occur following this type of fracture.

JAMES J. CALLAHAN

If you were afflicted with a hip ailment, I am sure that your main desire would be for relief of pain and a useful hip with a minimum amount of deformity or disability. Arthroplasty of the hip is usually performed with these precise aims: relief of pain and increased function of the limb to facilitate walking. Arthroplasty is therefore necessary in any of the following disorders: malum coxae senilis, suppurative arthritis, Legg-Calvé-Perthes disease, old slipped capital femoral epiphysis of the femur, congenital or acquired dislocation of the hip, congenital aplasia of the acetabulum, aseptic necrosis of the head of the femur after a fracture or dislocation, an osteochondritis dissecans of the head of the femur, a fracture of the acetabulum (especially the posterior lip) and a central dislocation in which the head protrudes into the acetabulum.

In recent years there has been a plethora of replacements or prosthetic devices. The disadvantages of such prosthetic types are becoming evident. Absorption occurs at the site of the metal and bone; decalcification of the proximal portion of the distal femur has happened; there has been loosening, and even breaking of the prosthesis as a result of flaws. Soft tissue contraction, excessive scar tissue formation and even bone formation following extensive incisions of the ilium have taken place. Individual susceptibility to metal and to resins has been a further disadvantage.

Errors in technic and surgical judgment may occur in any procedure. Numerous hip operations have been attempted, some with

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success, others with failure—failure usually because two essential requirements were not fulfilled: relief of pain and increased function at the hip joint.

It is interesting to note from the many operative varieties developed that apparently a standard procedure cannot be adopted. Modifications must be made according to circumstances. Of all the types of reconstruction operations, or arthroplasty, devised, however, the Whitman reconstruction, the Colonna reconstruction, the Albee reconstruction and the Smith-Petersen method have withstood the trials of time and, in most instances, have been successful.

A procedure is offered herein which has been satisfactory in my practice for over 20 years and which has been performed in over 70 cases. The results were not uniformly successful, but on the whole have adequately accomplished the major requirements, relief of pain and increased function of the hip joint. At this point, full credit is given to Dr. Royal Whitman and Dr. Paul Colonna whose procedures are essentially the same as mine, with this modification by me: removal of the lesser trochanter and a careful removal of the posterior portion of the upper femur to permit better fitting of the newly formed head in the acetabulum.

The method to be outlined may well be employed in every case in which an arthroplasty is contemplated, because according to a re-examination of poor results illustrated in published slides, photographs and roentgenograms by many surgeons, the lesser trochanter has impinged on the inferior border of the acetabulum. In many instances this type of complication has prevented full painless weight-bearing. Early in our own series, two patients with pain in the inguinal area were found, on later investigation, to have an articulation between the lesser trochanter and the inferior border of the acetabulum, invalidating an otherwise good arthroplasty.

I have been particularly impressed with the absence of pain and the increased function resulting from this recommended operation, which combines the anatomic with the functional and results in a normal articulation without the use of any foreign material.

Operative Procedure

Preoperative approach—The osteoarthritic patient must undergo an evaluating examination. The surgeon must be confident that the patient will cooperate fully and really wants to get well.

Roentgenograms are then taken to rule out involvement of the opposite hip, because frequently both hips will be afflicted, particularly, in the presence of osteoarthritic changes. When a young patient has stiff hips, complications usually are caused by the lower lumbar vertebrae and sacro-iliac, while in the elderly patients, the causes are usually the lower lumbar vertebrae and the opposite hip.

The leg to be operated on is placed in traction for from five to seven days. During that time, an evaluation of the patient's general physical condition can be made. And again, both lateral and anterior-posterior roentgenograms are necessary to provide a true picture of the pathologic condition present.

Technic—1. With the patient under a general anesthetic, a Callahan incision is made to expose the pathologic process.

2. The greater trochanter including the posterior bulge is removed to permit an accurate fit of the shaft in the acetabulum.

3. The head is now exposed so that excess bone can be removed.

4. The head is then shaped to fit rather loosely in the acetabulum.

5. All debris is removed from the acetabulum.

6. The lesser trochanter is removed. This, in my opinion, is one of the most important steps, because it will insure articulation without any impingement of the lesser trochanter on the inferior portion of the acetabulum. This is especially significant when there has been much absorption of the neck of the femur according to roentgenographic evidence.

7. All synovial villi are surgically removed.

8. The head is replaced in the acetabulum. The capsule usually is not closed in these cases.

9. The greater trochanter is then reattached lower on the femur with either silk or catgut.

Nonunion base of neck of left femur.

At this time, it is imperative to make sure that the weight-bearing line is maintained, so that there will be no inversion or eversion at the knee to cause strain or pressure at the knee.

10. Muscle and skin closure is accomplished.

11. A unilateral body cast is applied just below the opposite axilla to below the knee or to the lower part of the affected leg.

12. Skin sutures are removed in approximately 10 days.

13. The patient is placed on the fracture table in the correct position; the cast is removed, and another unilateral body spica is applied.

14. As soon as the cast is dry, the patient is permitted to be ambulatory. The cast is worn for two or three weeks.

15. The entire immobilization is then removed, and full weight-bearing is permitted.

16. Intense physical therapy is instituted, and it is very essential.

17. The presence of absorption of the neck of the femur should be further investigated by taking roentgenograms with the patient in a standing and weight-bearing position; in

Plastic operation because of absorption of neck; immobilization with two screws.

End result.

Destructive arthritis.

Postoperative oblique.

other words, a vertical Bucky's roentgenogram, because these roentgen rays offer the only method of determining whether the lesser trochanter really impinges on the undersurface of the acetabulum. Most roentgenograms made following an arthroplasty are taken with the patient lying down and in reality do not show the true condition.

No attempt is made to correct the shortening. Elevation later not only helps overcome any Trendelenburg appearance but also assists in the formation of a better joint.

Applicability of Procedure

1. This outlined operation has likewise been performed for nonunions of the neck of the femur. The scar tissue is left on the proximal portion of the distal fragment. This soft tissue, or scar tissue, acts as an interposition operation and has been successful when early weight-bearing was accomplished.

2. In patients over 70 years of age with a fracture of the subcapital area of the neck of the femur and in whom circulation is extremely poor or even absent, reconstruction at this point has become a satisfactory preliminary procedure.

Anterior-posterior, postoperative.

Coxa magna following juvenile disturbance.

Postoperative.

3. In osteoarthritis, this operation has been used with varied success. The cartilage is left on the acetabulum or the head as an aid in forming a new joint or articulation. The opposite hip must be watched. In some cases, it has been necessary to operate on the other hip after there is good weight-bearing by the hip involved in the first operation.

4. In fractures of the neck of the femur when the head is viable and when it is not adherent to the acetabulum but there has been absorption of the neck, the greater trochanter and lesser trochanter are removed; the proximal and distal ends are freshened at the fracture site, and an approximation is secured by means of internal fixation. Although this procedure does cause a certain amount of shortening, it has resulted in an excellent union of bones in most cases.

5. This type of arthroplasty is especially recommended for the early middle-aged group, because it can be used as an intermediate surgical procedure which will not preclude later surgery in the event of failure or if later a replacement prosthesis is indicated. To date, however, it has not been necessary to perform additional surgery, except when the lesser trochanter was not removed during the preliminary procedure.

6. Age is not a contraindication to this procedure, provided that the patient's health has been carefully evaluated.

Importance of Weight-bearing

My adoption of the procedure described occurred as a result of an error or failure. I was attempting to secure an arthrodesis in a dislocation of the hip which had been acquired 40 years previously. The patient had a painful hip with marked restriction of motion. At the time of surgery, both the head of the femur and the newly formed acetabulum were completely denuded of articular cartilage, and the two rough surfaces were accurately approximated. Internal fixation was not used. Following closure of the soft tissues, a unilateral body cast was applied. At about that time, Boehler had popularized the walking iron, which I incorporated in the second body spica applied. The cast remained on for approximately three months with the patient bearing weight most of the time. On removal of the cast, there was excellent hip motion without pain. The patient was grateful, but I was disappointed. I watched the results in that patient for more than 10 years. She has had an excellent result without pain. She is able to do her housework and is happy with the condition of her hip.

This error led me to the conclusion that weight-bearing is important in depositing a new fibrocartilage at the articulation. This conclusion is substantiated by the observation of others. In Sir Robert Jones' lecture,

"The Physiology of Arthroplasty," the author demonstrated that the type of joint secured after arthroplasty and the type secured after destructive processes when ankylosis did not occur were histologically and microscopically identical. The work of G. A. Bennett and Walter Bauer, published in the *American Journal of Pathology* in 1931, supports the view that weight-bearing has a decided influence on articular cartilage and on the formation of articular cartilage. Smith-Petersen also stated in the *Journal of Bone and Joint Surgery*, January 1947, "The lesser trochanter sometimes comes into dangerous proximity to the anterior lip of the cotyloid notch, particularly with the extremity in adduction. Subperiosteal excision of the lesser trochanter, with the distal expansion of the iliopsoas attachment left intact, prevents such mechanical impingement."

Acetabular aplasia, severe pain and loss of function.

Postoperative oblique.

Anterior posterior postoperative.

Aseptic necrosis of head with collapse of head following Smith-Petersen pinning.

Postoperative oblique.

Anterior-posterior postoperative.

Summary and Conclusions

1. A 25 year review of the literature reveals that only one writer has mentioned the possibility that the lesser trochanter might be a source of disability and that, therefore, it should be removed.

2. Re-examination of published roentgenograms affirms that many failures are due to the proximity of the lesser trochanter to the inferior portion of the acetabulum.

3. Roentgenograms taken under weight-bearing are essential to determine the position in the acetabulum, especially if the lesser trochanter has not been removed, and the patient has pain.

4. Early weight-bearing is essential to the success of the procedure described.

5. The procedure is recommended for the early middle-aged group; nevertheless, there are no contraindications to its use even in elderly patients, provided that a careful medical evaluation is obtained beforehand.

6. Prosthetic replacement operations can always be resorted to later, if this procedure fails.

7. Patients should be selected who are cooperative and show a will to walk.

8. Recognition of the pathologic status of the opposite hip is important. The patient must be informed of this complication, if it is present.

9. The importance of physical therapy cannot be overstressed.

10. Shortening should not be compensated for early, but the patient should be allowed to work the new joint while the leg is short so as to increase the efficiency of the joint and encourage the deposition of fibrocartilage.

11. The results of an arthroplasty after a long period of immobilization for nonunion are not as good as in early cases because of the complication of fibrosis of the various joints and muscle atrophy accompanied by vascular changes in the extremity. Such complications present a difficult problem in muscle rehabilitation, and, in my opinion, the results of surgery never fully measure up to the results the patient or surgeon anticipates. With this in mind, procrastination should be avoided and early surgery encouraged.

Old slipped femoral epiphysis—marked disability, pain.

Postoperative.

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DIAGNOSTIC CLINIC

Urinary Calculus Disease

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The problem of ureteral calculi is concerned not so much with the size of a stone as how rapidly it is progressing. Stones that reach the lower ureter in a day or two are on their way out; those that hang in the upper ureter have a long and hard journey ahead and are best removed surgically.

IN this discussion of urinary calculus disease, I will concentrate on what is the most interesting and common clinical problem of stones, that is, the ordinary ureteral calculus.

Through the courtesy of the resident staff at the Veterans Hospital at Hines, we have three very interesting patients here. After presenting their histories, I will discuss some illustrative films that emphasize important points in connection with these cases.

This first patient is a young white man, a veteran, who has had a history of stones that goes back some length of time. Even while he was in the service he had some pain in his left side, but apparently the situation was not pressing at that time.

Shortly after he came out of the service, I think in 1946, he came to the Veterans Hospital with some signs and symptoms suggesting a left renal stone, but none was demonstrated. However, in 1949 he folded up with a very severe colic and was admitted to the Veterans Hospital where a stone was found in the extreme upper left ureter.

The intravenous urogram made at that time demonstrated a shadow lying in the line of the ureter, which is important diagnostically. More interesting still, it showed that dye was coming through the kidney, indicating that, for the moment at least, the kidney was still functioning. One can also assume that the stone had not completely occluded the ureter and was, at the moment at least, not a serious threat to that kidney.

The stone was removed surgically and the patient had an uneventful convalescence. Last week (late October 1953) he was readmitted to the hospital with another attack of typical left colic. Once again a small stone can be seen lying in the upper ureter, and the uro-

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gram shows that the shadow is in the line of the ureter and that the kidney is functioning.

I will reserve my comments concerning the management of this type of stone in the upper ureter until I discuss the illustrations.

The next patient is a Negro veteran who came to the hospital at Hines some six weeks ago because of his present problem. He said that he had had some distress from time to time in his left back but nothing that was ever sufficiently severe to require any examination or treatment. At the time he developed the very sharp pain, he was brought into the hospital in considerable agony and required morphine. Examination revealed the presence of a stone, in this instance well down in the lower right ureter within an inch or two of the urinary bladder.

The question of surgery was considered, but as the patient was under age, it was necessary to wait until his folks could be reached for permission to operate on him. As a consequence, for the next four or five weeks, the usual efforts were made to stimulate passage of the stone; catheters were left in overnight and some oil was injected, all in the hope that this might help the stone to pass. But it did not.

Finally, because the excretory urogram had begun to show some stasis in the upper urinary tract, it was felt that the stone should come out and he was operated on and the stone was removed. He is now convalescing (I think this is the tenth or twelfth day); his drain is still in, but it is being removed gradually.

The fact that there is a stone in the lower ureter here, in contradistinction to one in the upper ureter in our other patient, poses a most interesting question. I think it is clearly understood that the majority of patients who develop renal or ureteral colic in the course of passing a small stone do best with ordinary expectant treatment and with occasional injections of morphine to take the edge off their severe pain. I am confident that those of us whose work is limited entirely to urology see a relatively small percentage of ureteral stones, because the patient and his family physician handle the situation quite adequately alone. Most stones are small stones; they come down fairly rapidly; the pain is, of course, readily controlled by medication, and, with a few days of tolerance and watchful waiting, these stones ordinarily pass. It is only when they obstruct or hang in the ureter at some point for an inordinate length of time that they are real problems, such as the cases we have here.

The third patient illustrates something of the answer to that question concerning the likelihood of recurrence of stones and the possibility of their prevention.

The patient is an elderly man, who originally came to the hospital with typical symptoms of prostatism: difficulty in voiding, frequency of urination, heavily infected urine, and considerable retention of urine. At that time, some three years ago, he had a transurethral resection which answered his obstructive problem very nicely. The point of interest to us is that at the time he was first admitted three years ago, the ordinary scout excretory urogram showed that the lower ureters on both sides were quite dilated. Whether this was a simple anatomic defect or whether it had something to do with his prostatism is not clear to me at the moment, but the fact remains that there was stasis and dilatation in his two ureters. There were no stones at that time. However, when he returned a year later, because of persistent pyuria, a large stone was found lying in the lower ureter.

The retrograde pyelogram showed the degree of dilatation of the ureter and the stone lying within it. That stone was taken out surgically.

He came back in another year with recurrence of severe pyuria. At that time stones were found in the dilated lower ureter on the other side.

Without going into further details of this case, I want to call your attention to the fact that in this man we have been able to watch the formation of stones in a part of his urinary tract in which there was dilatation and stasis of urine with the inevitable presence of chronic infection. These circumstances have considerable to do with the answer to the question of how to avoid having stones form again.

The question of the management of stones

in the ureter is really challenging, because there are times when it is perfectly safe and proper to permit a stone to find its own way out, and there are other times when it is very important that surgical interference or some other acceptable method be employed to remove the stone. Figure 1 illustrates essentially the same problem that occurred in our second patient. Stones were found in the lower ureters, within an inch or two of the urinary bladder. The first x-ray film is usually taken during the first three days after the onset of colic. As in each of the three cases illustrated, the stone may be quite sizable. However, it is most important to note that the stone already has traveled four-fifths or more of the length of the ureter in a relatively short time. Regardless of their size, stones that have found their way down to the extreme lower ureter within a day or two of the onset of colic are stones that are pretty well on their way and, usually, with a bit of patience and tolerance, will pass themselves. If not, very frequently they can be urged along by some transurethral or cystoscopic manipulation, such as was employed in one of our patients.

It is not often that these low ureteral stones have to be removed surgically. I am not sure that the stone in our second patient would have had to be removed surgically, though I think you all appreciate the necessity, particularly in military personnel, of having some definitive answer to the problem reasonably quickly. In this case it was certainly a very safe and probably very sane procedure to remove the stone surgically.

Sometimes stones of considerable size can be manipulated when they hang for an undue length of time in the lower part of the ureter. Figure 2 (first view) shows a fairly sizable stone that was within an inch or so of the urinary bladder in a woman. Passing two or three ureteral catheters (figure 2, second view) proved, first, that the stone was quite

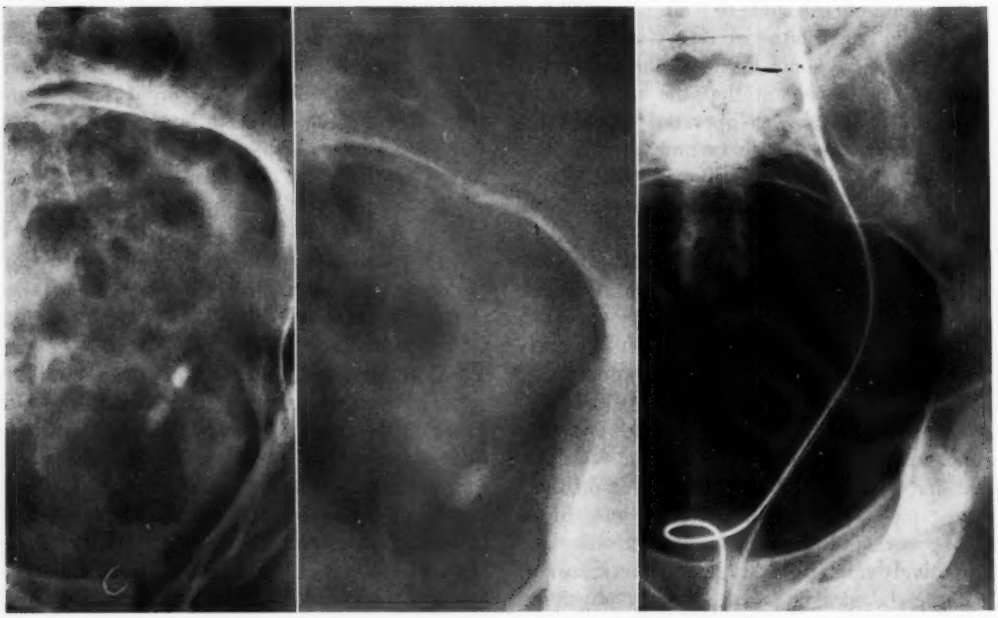


FIGURE 1. Three cases of stone reaching the lower ureter soon after the onset of colic. Stones in the first two cases passed spontaneously; that of the third case passed soon after withdrawal of catheters left in the ureter overnight.

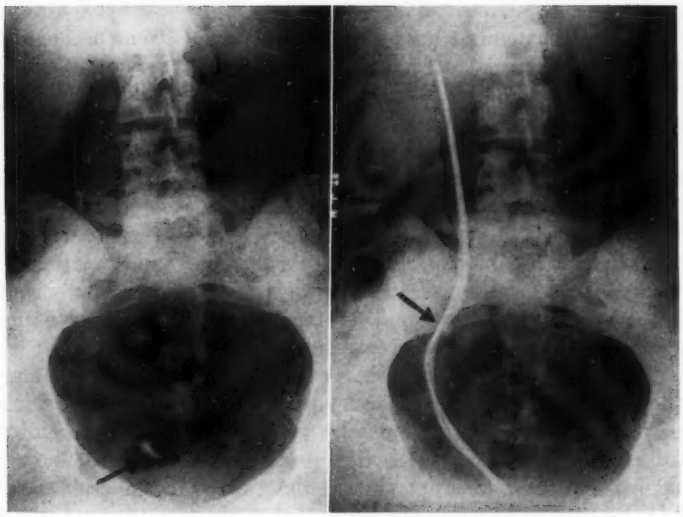


FIGURE 2. A rather large ureteral calculus quite freely movable in the ureter and passed promptly after inlying catheters.

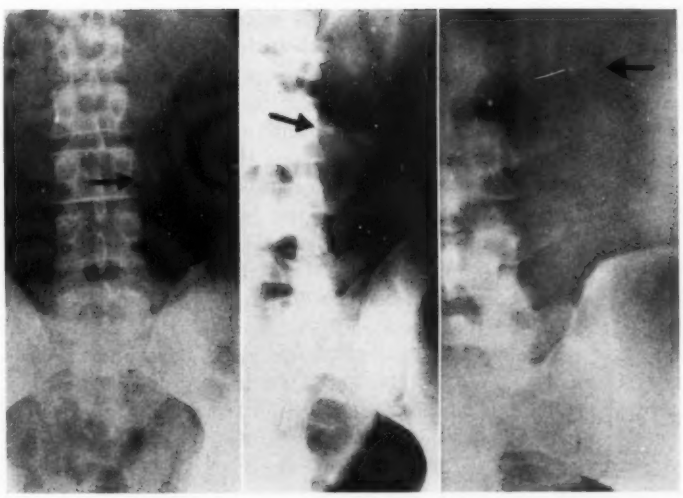


FIGURE 3. Three cases of stone arrested in the upper ureter suggesting that spontaneous passage would be slow and difficult. In all three surgical removal was elected as the less disabling and dangerous procedure.

mobile. It was therefore not surprising that, within an hour or two after the catheters were withdrawn, this woman's stone was found in the bedpan, simply illustrating the fact that even sizable stones sometimes pass down the ureter and out without very much difficulty. It is not so much the size of the stone as how rapidly it progresses that provides a clue as to whether it is wise to be conservative or whether it is more important to interfere surgically.

The problem presented by the first patient discussed is illustrated in figure 3. You will recall that patient had had two stones re-

moved surgically from his upper ureter.

The three patients whose films are shown in figure 3 all had stones. I think you will agree that they were all reasonably small stones, but they hung in the upper ureter. They had not traveled down into the lower pelvic ureter, as had those in figure 2, despite the fact that there had been two or three days of colic.

In my teaching in connection with the management of ureteral stones, I have always said that a stone which is found in the upper ureter on the first x-ray, regardless of its size, should be removed surgically, except in a doctor. And the exception is very pertinent. As you well know, a patient who folds up with stone colic (and I think very properly) is given some morphine and carried along for a day or two to see just what the course of events will be. That means he has his x-ray on the second or third day after his colic begins. That is not true of a doctor. If he has a lot of pain on one side and goes to his microscope and finds a few blood cells in the urine, he has an x-ray within two or three hours, and two or three hours is too short a time for a stone to prove how rapidly it can and will pass down. Therefore, except for doctors, if a stone is still found in the upper ureter two or three days after colic starts, as was the case with both stones in our first patient here, there is no question in my mind (and I think this is the generally accepted procedure throughout the profession) that the stones should be removed surgically. Determination for surgery ordinarily should not be based on the size of the stone, but on the fact that it simply is not moving as it should. If a stone cannot readily traverse the larger upper ureter, one can very well anticipate that if and when it finally does work down to the lower ureter where the lumen is definitely smaller, the problem of extraction is going to be unusually difficult.

At one time we were more enthusiastic than we are today about the idea of manipulating ureteral stones by one method or another in an effort to extract them or to hurry their course along. Apropos of that, I would like to discuss a series of four films that were taken on a patient of mine many years ago over a period of about three months (figure 4).

The patient came in the day after Christmas; he had left colic with quite a sizable stone in the upper left ureter. In those days, as I say, we were a bit more enthusiastic about manipulating ureteral stones, and I did cystoscope this man. In fact I cystoscoped him five or six times between the day after Christmas and the third of March, which was the day his stone finally came out. You can see the progress of the stone; it first moved down a half inch; next it was a little lower, across the sacro-iliac joint; then it came into the pelvic ureter, and finally it passed out, much to the gratification of the patient and myself. During those three months this patient had had considerable expense and a great deal of distress in connection with his recurrent colic and frequent cystoscopies. We were quite elated, however, because we had succeeded in getting the stone without surgery.

Ten years later, the same man had a skull fracture in Madison, Wisconsin, and was taken to one of the local hospitals. In the course of his stay there, his urine was found to be loaded with pus. A flat x-ray film (figure 5) showed the end result of the three months of effort, by repeated cystoscopies, to try to remove a large stone which I now know should have been taken out the day it was first found in the upper ureter.

Incidentally, there is an addendum to this story because this man is now at the Veterans Hospital at Wood, Wisconsin, where I operated on him last Friday. The old left kidney is utterly dead and in the meantime the right kidney has filled completely with stones. He has very severe uremia and is just barely alive today. Whether or not the retention of that old rock in his left side (he would never permit surgery until the other day) and the associated pyuria had something to do with the formation of the stones in his other kidney, I do not know. However, I am quite sure that this whole series of events, going on over a period of 22 years, was the very natural result of what I then thought was good procedure in trying to extract a high ureteral stone and avoid the necessity of surgical removal.

I want to mention the excretory urogram in connection with stones of the urinary tract. It can be very useful or it can be very confusing. Sometimes one can make a serious error by reading into the excretory urogram (the "intravenous pyelogram," if you prefer) information that should not be included.

In general, in connection with stones in the urinary tract, as well as in all other urologic pathology, it is pretty much a truism that when dye is seen coming through a kidney promptly and in good concentration, one can be quite certain that the kidney is functioning well. I think that is a very safe conclusion to make from an intravenous pyelogram alone. I would caution any of you who need it, however, that the converse is absolutely not true. If dye does not appear promptly and in good concentration in one kidney or the other, it only means that, for the moment, that kidney isn't working; it tells nothing at all of what it did an hour ago or what it will do tomorrow. We see evidence of that frequently. For example, figure 6 is an intravenous pyelogram of a man with a small stone that has lodged temporarily in the upper ureter. The dye has come through the other kidney promptly and in good concentration, but no dye at all was seen on the stone side. It would be a very dangerous and unwarranted assumption to conclude that, because there is no dye coming through, the kidney is injured. It simply means that it isn't working at the moment.

After that stone was removed (it was removed surgically—in fact, it was one of the three in figure 3) excretory urograms taken when the patient left the hospital showed that

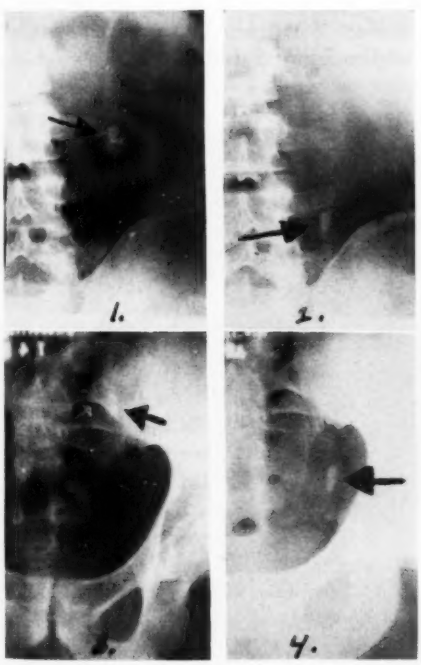


FIGURE 4. Four x-rays taken over a period of three months showing slow progress of a large ureteral stone despite frequent cystoscopic manipulations.

FIGURE 5. Giant renal calculus 10 years later (same case as figure 4).

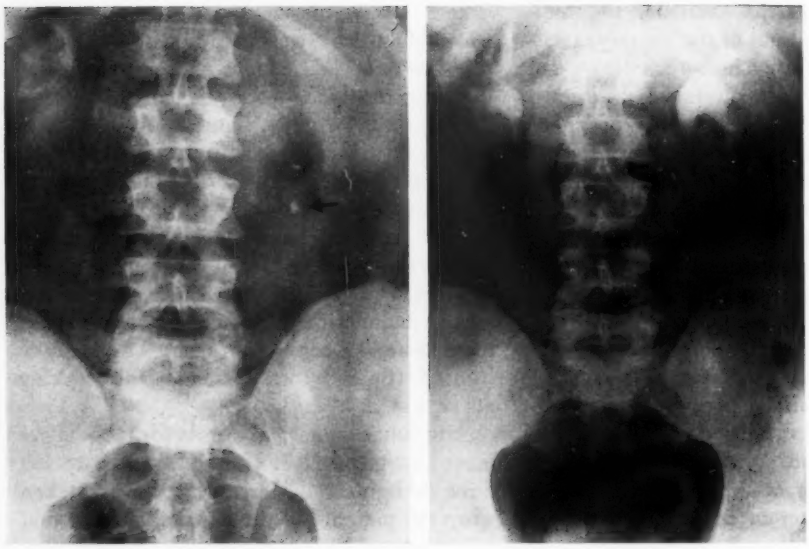


FIGURE 6. The excretory urogram before and after surgical removal of a high ureteral stone. Absence of opaque medium above the stone might be mistaken to mean the kidney was dead.

the kidney was fine, both functionally and anatomically.

As I stated previously, it is most important sometimes, by the use of the excretory urogram, to learn that there is function present. For example, figure 7 is from the case of a

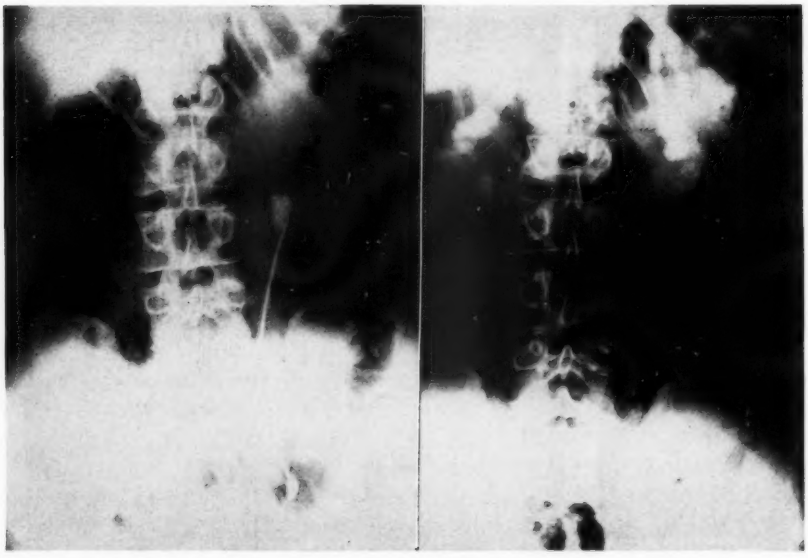


FIGURE 7. The first view shows the catheter tip arrested by the stone and opaque medium regurgitating, both suggesting that the stone was completely obstructing the ureter. Second view shows substantial function remaining, dictating removal of the stone rather than the kidney.

man who had a very protracted history of severe left-sided pain. He was a Christian Scientist and for a long while sought no medical relief at all. I saw him some three or four months after he had had a lot of left-sided pain, chills and fever. The flat film showed a large stone in the upper ureter. When I inserted a catheter which couldn't get past the stone, and, more particularly, when I injected some opaque medium through the catheter and none of it ran up but all regurgitated back down the ureter, I felt quite sure that his kidney probably was not functioning and that the situation was one in which simple nephrectomy was the proper thing to do. However, as a matter of routine, excretory urograms were made, and the second view shows a fairly good concentration of dye in the renal pelvis, though the pelvis is quite badly dilated from the long-standing obstruction by the stone.

I have learned, as I know all of us who have followed this sort of work long have learned, not to be too startled at dilatations of the upper urinary tract when there is a definite obstructive cause for them.

Reassured by the presence of function in that kidney, despite its size and my other findings, the stone, instead of the kidney, was removed. Figure 8 is a retrograde pyelogram taken of the same man six years later. I could also show you the excretory urogram demonstrating the considerable recovery of renal function that followed. However, the retrograde pyelogram shows the almost unbelievable way in which a dilated kidney will return to a reasonably normal shape. Now, a number of years after surgery, the patient has a perfectly fine kidney, thanks to the information obtained from the excretory urogram.

While it is a little aside from the subject of ureteral stones, I think it might be interesting to consider briefly the problem presented by stones other than ureteral stones. After all, the question of stone, as far as the patient is concerned, involves several things. First is the question, "Why did I have a stone in the first place?" Once that is answered, if it can be, and it usually cannot, comes the question, "What is the problem and how is it to be managed?" Finally, there is the question, "Now that it is out and I am through with this stone, how can I avoid having another one?"

FIGURE 8. A retrograde pyelogram taken six years after those seen in figure 7 and showing the anatomic involution that followed removal of the stone. Complete functional recovery was also demonstrated.

It would take too long to discuss intelligently here the whole question of the etiology of stones. Suffice it to say, however, that there are two or three things that always should be remembered by both the physician and the patient who forms stones. In the first place, if there is any one thing that will almost surely invite the recurrence of stones, it is stasis of urine. It would be perfectly silly for anyone to open a bladder and remove a stone when there is a large prostate gland causing obstruction and chronic retention of residual urine in the bladder cavity. It would be equally silly to take a stone from the kidney pelvis if the pelvis itself is dilated as a result of a ureteropelvic obstruction—in other words, in the presence of hydronephrosis. If there is stasis of urine and a stone is to be removed,

the underlying cause of the stasis also must be removed. There is nothing that so readily invites the occurrence or the recurrence of stones as stasis of urine.

Next on the list is the presence of chronic infection. Infection changes the urine in ways that invite crystallization and stone formation. It leaves a lot of debris that readily forms a nidus on which crystals can form. It changes the *p*H and the colloidal chemistry of the urine and, by so altering its chemical and physical properties, plays a large role in stone formation. Infection must be done away with, if at all possible, if one is to answer the question of how the reformation of a stone can be avoided.

Finally, the patient himself can keep his urine diluted by drinking quantities of water the rest of his life. I think we have put our finger now on the three important everyday things that bear upon the formation of stones: (1) stasis of urine, (2) persistent infection and (3) the dilution of urine to reduce the likelihood of crystallization.

I have already discussed the problem presented in ureteral calculus disease. Let us consider the kidney itself. In figure 9 the retrograde pyelogram shows little stones in the calyces. These are perhaps the most innocent, unimportant stones that a human body can carry; they are little stones that are trapped out of the way in the little calyces. These stones have very little tendency to grow; sometimes they are borne throughout a lifetime without materially increasing in size. As long as they are trapped out of the way and can't get caught in the stream and started down the ureter, they cause very few symptoms or material damage to the kidney. For that reason, if for no other, they are usually left alone. There is still another reason why they are normally left alone. Any surgeon who tries to find those two stones had better have a stone or two in his pocket, because he may spend the forenoon in the operating room and not find them in the patient.

The most dangerous stone that a person can have is one that is too large to fall into

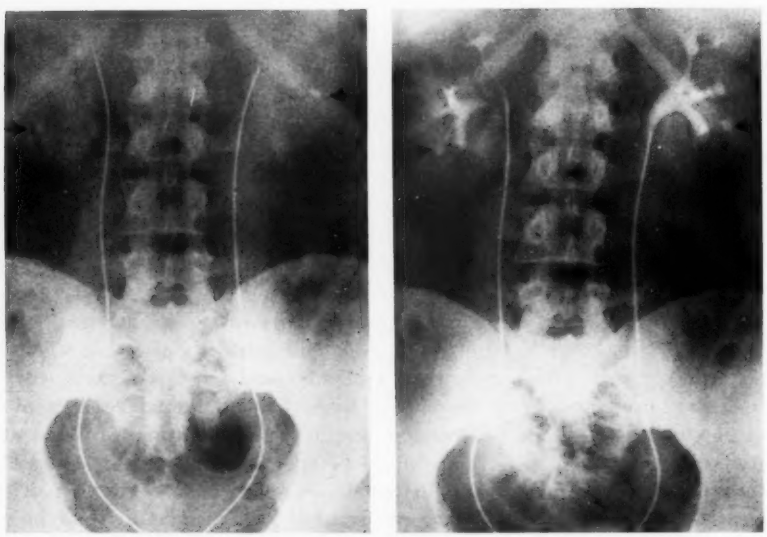


FIGURE 9. Plain KUB and retrograde pyelogram showing a small stone strapped off in a small calyx of each kidney. This type of renal stone is quite symptomless and usually borne indefinitely with little or no bother.

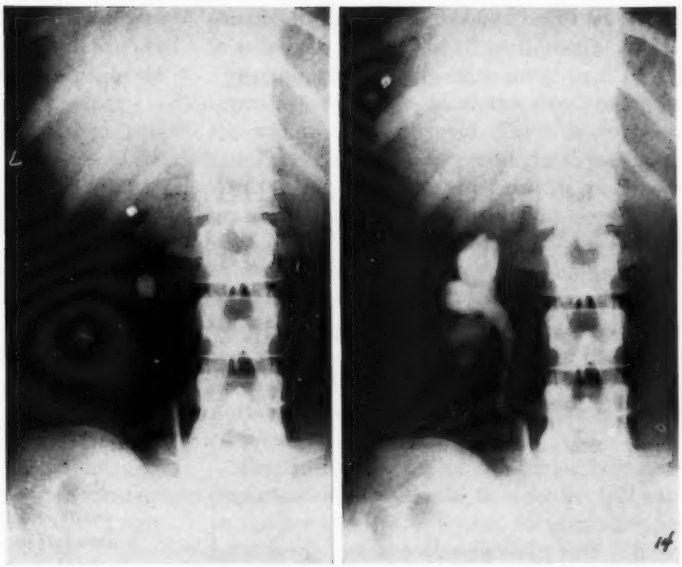


FIGURE 10. Illustrating the ball-valve action of a large single pelvic stone threatening the ultimate destruction of the kidney.

FIGURE 11. The excretory urogram taken years after removal of the stone seen in figure 10. Complete anatomic and functional recovery followed pelviolithotomy.

the ureter and thus precipitates a clinical situation that demands some answer. This type of stone is sufficiently loose and free in the renal pelvis to fall readily against the orifice of the upper ureter, obstructing it. Those of you who understand the principle of a ball valve will recognize what I am trying to say. That type of stone will roll into and then fall away from the orifice, periodically producing an obstruction that gradually damages the kidney but never blocks it off completely. It is this mechanism of prolonged, incomplete obstruction that causes hydronephrosis and, finally, complete death of the organ.

The same type of stone in a patient in whom the process was even more advanced is shown in figure 10. Again we shouldn't become too excited about dilatation of the renal pelvis or even an obvious decrease in renal function, if we can remove the cause of the obstruction and permit the kidney to drain freely again. An excretory urogram (figure 11) made several years later of the same patient proved that the kidney had recovered quite completely, functionally and anatomically, despite the degree of dilatation that had developed.

DIAGNOSTIC CLINIC

Adenoma and Carcinoma of the Thyroid

GEORGE E. CRILE, JR.

Cleveland Clinic, Cleveland

Most enlargements of the thyroid gland occur in older people and are the result of involutional changes in the thyroid. These nodules are not premalignant, and unless they become large or toxic do not require any treatment.

In younger people, however, and in those who have firm discrete tumors of the thyroid or enlarging tumors of the thyroid, serious consideration should be given to the possibility of cancer. If operation is performed, it should be designed to cure cancer if present.

Some enlargements of the thyroid are due to thyroiditis, and are amenable to medical treatment.

GEORGE E. CRILE, JR.

In the Great Lakes area approximately 5 per cent of adult women, on careful examination, will prove to have palpable enlargements or nodules of their thyroid glands. Alarming statistics published in the literature state that anywhere from 5 per cent of the nontoxic nodular goiters all the way up to 25 per cent of solitary nodules of the thyroid will prove to be cancer. Which of these large numbers of people who have palpable nodules in their thyroid glands should be subjected to operation? That is the clinical problem which confronts us. It is the question of when to advise a patient to have a nodule in the thyroid removed.

The prophylactic indications that we used to consider, such as the danger that the patient might develop hyperthyroidism and that that, in turn, would cause difficulty with the heart and make operation dangerous, can largely be discarded today, because we have effective physical and medical means with radioactive iodine and the antithyroid drugs for controlling hyperthyroidism and making it safe to operate if necessary or desirable. So we really come down to this one basic question: Which of these enlargements of the thyroid are potentially malignant in that they may ultimately turn to cancer or might be cancer now?

There is no black and white answer to this problem. Unfortunately, most older people, most older women particularly, have abnormalities of the thyroid. The pathologists will tell you that it is practically impossible to find a normal thyroid in women beyond, say, 55 or 60 years of age. They all have involutionary nodules of greater or lesser size, and, cer-

Presented before the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago.

tainly in the older age groups of women, these nodules are common, running much higher than the 5 per cent that are palpable in women who live in the Great Lakes area.

Are these nodules to be considered premalignant? The answer is probably not, because the incidence of cancer of the thyroid as a cause of death is extremely low; it ranks about seventeenth in the list of cancers and is only one thirty-seventh as common a killer as, for example, cancer of the breast. Probably just the mere presence of a nodule is not sufficient indication in all cases to require thyroidectomy. If we were to adopt the principle that every palpable nodule should be removed, the scale on which surgery would have to be performed would be quite frightening, because it would mean a very high percentage of the older people in the country would have to have prophylactic thyroidectomies.

How, then, are we to establish the points which indicate danger? In the first place, there is no question statistically, or in any other way, that a solitary tumor is the most dangerous tumor. This, again, gives support to the theory that it is not a transformation of a benign nodule to a malignant one, which is of importance in cancer of the thyroid. In a multinodular goiter, where there are dozens of adenomas present, you would expect a much higher rate of transformations to malignancy than there would be in a solitary adenoma; yet, it is in the solitary tumors of the thyroid that we predominantly see cancer of the thyroid at the time of operation.

Most cancers of the thyroid do not originate in adenomas; they are cancers from the first. Most cancers of the thyroid originate in otherwise normal thyroid glands. They may be extremely slow growing, so that through the years a sort of myth has grown up which says that because a tumor has been known to be present in the thyroid for 5, 10 or 15 years and is then removed and found to be malignant, there was a transformation from a benign tumor to a malignant tumor. Actually there is small evidence to suggest such a transformation, nor, at the time of pathologic examination, do we see adenomas which are partly benign and partly malignant; they are usually homogeneous tumors, each of which is either all benign or all malignant.

Certainly we can gain a great deal of information clinically from the consistency of the nodule in the thyroid. There is no question that almost all cancers of the thyroid feel hard or firm. One must distinguish, just as in examination of a breast, between a deep-lying, hard tumor which feels soft only because of overlying tissue and a superficial tumor which feels hard because it is hard and is close to the surface. A deep tumor in the thyroid may feel soft unless it is examined with particular care. The firmness of the tumor is most important in respect to the establishment of a suspicion of malignancy.

The solitary nature of the tumor is just as important in the thyroid as it is, we will say, in the breast. In the breast, for example, we have many patients who come in with diffuse, bilateral, cystic disease. We know from experience that these multiple nodules throughout all of both breasts, where there is no nodule which is any different from the other, are much less apt to be malignant than is a single nodule in an otherwise normal breast. Therefore, the very presence of multiple nodules is some evidence against that particular thyroid gland's having a malignant tumor in it.

Since the incidence of malignancy is relatively so low in a multinodular goiter as compared with a solitary tumor, there is little indication to remove a multinodular goiter routinely as a prophylaxis against malignancy. But the presence of an enlarging adenoma, suggesting the possibility of malignancy, or the hard consistency of one of the adenomas should raise the possibility of one of these tumors being malignant and is an indication for operation.

Let us apply these principles to a "ghost" clinic, and here I will have to call on your imaginations to bear with me for just a little, while I assemble a series of patients. The first patient, we will say, is a 15 year old girl, who has been brought in because she has a solitary firm tumor in the right lobe of her thyroid gland. There is no question whatsoever about the disposition of this case, because experience has shown us that the incidence of malig-

nancy in the thyroid, unlike almost any other organ, is inversely proportional to the age. A girl of 15 has no reason to have the involutionary changes in her thyroid which are so common in the oldest age group. If a girl of 15 has a solitary tumor in her thyroid, she probably has a true tumor, and there is about a 25 to 35 per cent chance of that tumor's being malignant. It should therefore be operated on not as an adenoma prophylactically to prevent it from becoming malignant, but as a carcinoma. That is true even if the mother said that the girl had had it ever since she was two years old and it had not enlarged. A solitary tumor in a child's thyroid, even if it has not enlarged for years, is clear-cut indication for a good, clean excision of all of that tumor and, preferably, all of the lobe on the affected side.

Suppose the next patient is a young woman, 25 years of age, who comes in with a solitary tumor. She probably has a true tumor of the thyroid because the involutionary changes of the thyroid, the multiple nodules of which this might be a dominant nodule if she were older, do not begin until later in life. Again, the 25 year old woman with a solitary nodule must be operated on as though we really thought the nodule was a carcinoma.

Then we have a woman, 45 years of age, who comes in stating that she has had a little goiter for several years, but now she has developed an enlarging nodule in the thyroid. Palpation of the gland reveals that the entire gland is enlarged and a little nodular, with nodules present on both sides, but there is one dominant nodule which is bigger than the others. If this is large enough to be of cosmetic importance the indications are perfectly clear. Any woman who has a goiter big enough to be conspicuous and to make her sensitive, so that she wears necklaces and high necklines and dresses for the goiter instead of for herself, has a clear-cut indication for thyroidectomy. From the standpoint of malignancy, however, the chances of this nodule's being malignant are rapidly falling off, because the lump she is worrying about is probably the dominant nodule of a multinodular goiter.

The same is true in the older age group. If the patient is now 65 years of age and has a multinodular goiter, the chances of its being malignant are extremely small. Furthermore, if she says this nodule has been present for 5 or 10 years, the chances of cancer of the thyroid ever actually killing the woman, even if the nodule is malignant, are practically nil.

Thyroid Cancers

When we discuss cancer of the thyroid, we have to forget all of our preconceived notions about cancer. There are two distinct varieties of cancer of the thyroid. One type occurs almost exclusively in patients over 40 years of age, reaches the height of its incidence in the late fifties, and is just like any other type of cancer. It occurs mainly in older people; it has varying degrees of malignancy; it can be graded all the way from grade I to grade IV. Unfortunately, the most common type of cancer which occurs in older people is the highly undifferentiated, highly malignant type of thyroid cancer for which there is at present no known cure. This is a devastating disease which comes on with great rapidity; the patients usually seek surgical relief within a month or two of the time they first notice anything present in the thyroid. Only 20 per cent of these patients have any knowledge of a preexisting enlargement of the thyroid prior to the time of this rapidly enlarging malignant tumor. That is one extreme.

The other extreme is what we call the angio-invasive adenoma, a very slow-growing tumor which tends to invade blood vessels and may be present for many, many years. This usually occurs as a solitary nodule, and it is because of this that we routinely recommend the removal of a firm solitary tumor in all young adults and middle-aged people, and even in the older age group, when this type of tumor develops for the first time with a short history. It might be an angio-invasive adenoma and it should be removed.

But what about the other great group of thyroid tumors? The tumors which we have been discussing, the more malignant ones, we classify as nonpapillary tumors. There is another large group of tumors which are called

the papillary tumors. Unfortunately there is no better name for them. They should be called false cancers of the thyroid rather than papillary cancers, because not all of them are predominantly papillary. Many may be adenocarcinoma variants or follicular variants of papillary tumors where most of the fields examined in the microscope show an adenocarcinomatous arrangement, yet such tumors will behave clinically exactly like papillary cancers and will have an extremely low degree of malignancy.

These papillary cancers, which usually occur in young people and frequently in children, appear to arise from some form of a congenital rest. They do not kill rapidly. Most of them, I think, would not kill at all even if they were not surgically treated, but some of them will. Over a period of 15 to 25 years, some of them, particularly if they are poorly treated, will recur. Occasionally, they may metastasize and may cause death. For the most part, they are tumors of a low degree of malignancy which can be dealt with adequately by types of operations quite different from those required to cure the ordinary cancer which we think of in connection with squamous cell cancer or adenocarcinoma arising in other organs.

An important feature of papillary carcinoma is its ability to implant itself in wounds. If a papillary carcinoma is cut into at the time of operation, it may implant itself, recur locally in the wound and become inoperable. Furthermore, we know statistically that the incidence of distant metastases, chiefly to the lungs, is tremendously increased by incomplete local operations in which the primary tumor has been cut across. It appears that this type of trauma to the tumor opens vascular spaces into which tumor cells enter and then metastasize distantly to the lungs.

Papillary cancer of the thyroid is a problem of its own which requires an extensive local operation on the thyroid. It also requires a very extensive exploration of the cervical lymph nodes, to which this tumor very frequently metastasizes. It metastasizes early to the lymph nodes, but lymph node metastasis, even when extensive, does not mean incurability. We have seen a number of patients, some 10 now, whom we have had an opportunity of following from 5 to 17 years, who have remained well after removal of the primary tumor and up to anywhere from 20 to 40 involved lymph nodes in the cervical region and the superior mediastinum. This type of operation can be performed without mutilating block dissections, because the individual metastases are not invasive of muscle like a squamous cell carcinoma and because the intervening lymphatics are not involved. The main thing to do is to clear out the primary thyroid tumor and then to attack the groups of nodes to which metastasis takes place—to attack them and remove them in groups, not necessarily en bloc with uninvolved tissue like sternomastoid muscle. This is quite important, because the majority of these papillary carcinomas occur in young adults, usually in attractive young women and often in schoolgirls. Radical resection, the block dissection of the neck with sacrifice of nerves and muscles, with its attendant deformity and scar is a most disastrous thing to happen to a young girl, particularly when there is no need whatsoever for doing it. The published curability rates are actually higher following extensive operations in which attention is focused on the primary tumor and the zones to which it commonly metastasizes than by block dissection, an operation which is perfectly good for squamous cell carcinoma of the head metastatic in the neck, but which has nothing to do with the zone of metastasis of papillary thyroid cancer.

You can see, therefore, that we must know the natural history of the type of cancer with which we are dealing in order to plan cancer surgery.

The accompanying illustrations indicate some of the conditions I am discussing.

Figure 1 represents the middle-aged to elderly woman with a multinodular goiter. This type of goiter is a physiologic response to perhaps a combination of iodine deficiency, some congenital predisposition (because this type of goiter tends to run in families) and perhaps to the ingestion of some goitrogen.

This woman's thyroid is a mass of adenomas. You cannot perform a subtotal thyroid-

FIGURE 1. Multinodular goiter.

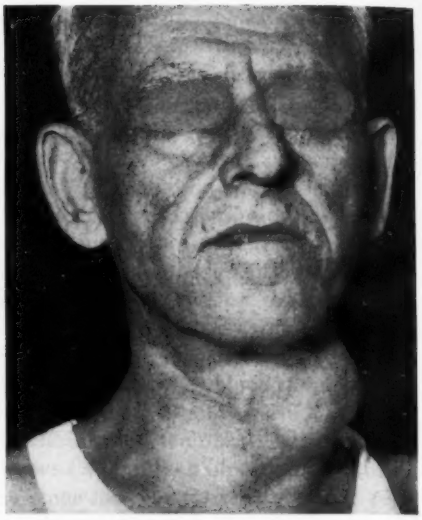


FIGURE 2. Solitary adenoma.

ectomy on this woman without leaving adenomatous tissue, because she has adenomatous tissue everywhere. The operation is done not to prevent cancer, since you would have to do a total ablation of the thyroid to remove all of this tissue, but merely to get rid of the great mass of tissue.

An entirely different situation is illustrated in figure 2. This is a solitary tumor of the thyroid in a man of middle age. Although he has had that tumor for 20 years, its long duration does not by any means exclude the possibility of malignancy. Tumors of low-grade malignancy, angio-invasive and papillary carcinomas, may persist for 15 or 20 years or a lifetime with hardly any enlargement at all.

Most of these solitary tumors occur in an otherwise normal thyroid gland. They are true tumors and they are important because they are indistinguishable from low grade cancers that show invasion of blood vessels and the potentiality of metastasis through the blood stream.

The type of tumor that occurs in older people is shown in figure 3. This man is younger than most persons who develop this tumor. He is in his mid-forties. Most patients

FIGURE 3. Undifferentiated carcinoma of thyroid.

who develop this rapidly advancing, hopeless type of cancer of the thyroid are in their fifties or even sixties. When they come in they do not need a doctor to tell them that something is seriously wrong, because these tumors enlarge very rapidly. No matter how early you get to them, it is impossible to cure

them. Local recurrences are the rule. We have just about come to the conclusion that operations in such cases actually spread the tumor more rapidly.

Note the skin metastasis. The patient also has pulmonary metastasis. This picture, incidentally, was taken within two months of the time that radical thyroidectomy and block excision of the structures of the neck was performed, and all of this grew back, all of these lumps, almost at once and while he was still under treatment with x-ray. X-ray is of no value in most cases of undifferentiated carcinoma.

Figure 4 shows a papillary carcinoma, a tiny primary tumor only a centimeter long, with characteristic lateral cervical metastasis, of the type which occurs in a young adult or in a schoolgirl. This is a favorable type in which a good clean excision of the entire lobe of the thyroid plus removal of the involved lymph nodes in groups like this with their surrounding fat is the treatment of choice. A good cosmetic result can be obtained and, usually, the entire low neck bilaterally can be satisfactorily cleaned out through a wide thyroidectomy incision. Occasionally an anterior sternomastoid incision is employed, and sometimes we clean out the entire lower neck and obtain a better cosmetic result by making transverse upper neck incisions to remove the upper metastases.

Another instance of what appeared to be an adenoma of the thyroid is shown in figure 5. The first picture was made in April, the second in June. In two months, the adenoma was gone after the daily administration of 3 gr. of desiccated thyroid.

What happened to that "adenoma?" Obviously it was not an adenoma. It was Hashimoto's disease, a type of lymphoid thyroiditis, struma lymphomatosa, which resembles a nodular goiter. It may be very asymmetric; it may have one area which is much more prominent than another. It is always called a nodular goiter if it is not properly recognized.

Characteristically, a middle-aged woman may come in stating that for the last few months she has noted enlargement of her thyroid. It feels like a multinodular goiter except

FIGURE 4. Papillary carcinoma with lateral cervical metastases removed through conventional thyroid incision.

for one thing: the thyroid lobes retain their shape and they are abnormally firm; the entire lobes bilaterally and the isthmus are firm and have a rubbery consistency. Another thing which makes you suspect it is a low basal metabolic rate, because most of these people have basal metabolic rates less than zero and many of them will have myxedema. When struma lymphomatosa is suspected, its presence can be confirmed by needle biopsy in the office, using the Silverman needle.

If these patients are given desiccated thyroid, an operation can be avoided. How desiccated thyroid works no one knows, but it is a fact that if the thyroid gland is put completely at rest by giving 3 gr. of desiccated thyroid a day, the enlargement very rapidly disappears in almost all of these cases.

Summary

Multinodular goiters are probably not premalignant. The incidence of cancer may be a little higher in patients with multinodular goiters than in the population at large, be-

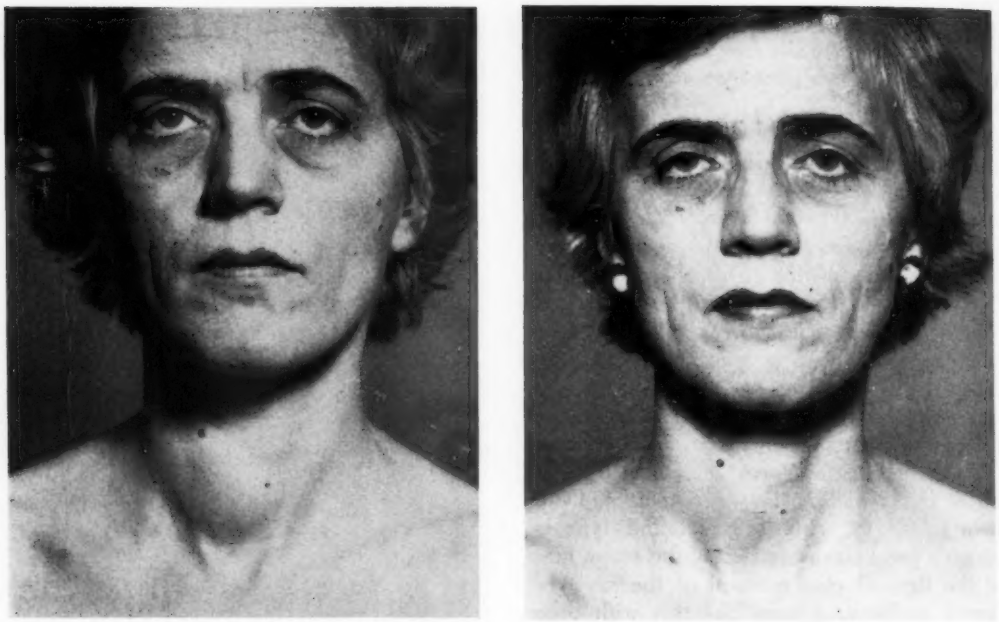


FIGURE 5. Struma lymphomatosa treated with desiccated thyroid 3 gr. daily for two months.

cause the goiters are bigger, there are more cells, and there is more possibility of their becoming cancerous.

Multinodular goiters are probably no more premalignant than multinodular breasts, and we don't do a bilateral simple mastectomy for every girl who has a firm nodular breast, nor do we routinely remove all thyroids from patients in all age groups who have multiple nodules in them. In the youngest age group one must be highly suspicious of solitary nodules. A nodule is of less importance in the oldest age groups. For example, let us say that a patient who is 65 or 75 years of age comes into your office for physical examination and you find a solitary nodule in the thyroid, maybe a little enlargement of the other lobe, but basically it seems to be a solitary nodule. If she gives a reliable history and says that the nodule has been there for 15 years, or if you can find some other doctor who says so, or from your own records you verify that the nodule has been there 15 years, it makes no difference whether it is malignant or not. If it is malignant, it is one of the little papillary things which grows so slowly that it is never going to bother her during her span of life. If it has not enlarged in 15 years or given any trouble, it is not going to give her any trouble for the next 15 years.

I don't say that it is a good thing to leave cancers in people's necks. Of course it isn't. If you have reason to suspect that a patient in the forties or the fifties has a thyroid nodule that may be malignant, by all means operate on it; but do it as a curative measure for existing cancer. Every week we see examples of patients from whom a nodule in the thyroid has been removed and, to the doctor's amazement, the pathologist says that it is cancer. Then the doctor worries; he sends slides around and asks for help. When you talk to him, you find that he did not completely excise the cancer. All he did was to cut most of it out, leaving the patient in a vulnerable position. If any operation is to be done, as it should be for solitary tumors in young and middle-aged patients and for selected nodules in older patients, let it be a good cancer operation the first time.

Certificate of Merit

Section on Internal Medicine

THE SCIENTIFIC EXHIBIT
AMERICAN MEDICAL ASSOCIATION
NEW YORK — 1953

Gout

ELMER C. BARTELS

Department of Internal Medicine, The Lahey Clinic, Boston

ONLY a few physicians, including such recognized authorities as Hench and Talbott, have "carried the torch," attempting to keep the medical profession aware of the commonly forgotten disease, gout. Most physicians consider gout to be extremely rare and should they consider this possibility in a given case, the diagnosis is made with great hesitancy owing to the uncertainty of the essential clinical characteristics of gout. Also, physicians have lacked enthusiasm for gout as its therapy has been thought to be unsatisfactory in most cases because even authorities on the disease have not been in complete agreement as to the proper method of treatment.

Gout is a common joint-disabling disease which must be considered in every instance of painful joint of the extremity. A carefully taken history is the best guide to its diagnosis since the pattern of the disease is characteristic, and the physical examination and laboratory findings may not be informative. Effective methods are available for treating acute gout and considerable advance has been made in interval therapy, which accomplishes restoration of the serum uric acid level to normal and thereby the avoidance of further attacks.

The common opinion regarding gout must be dispelled. It must not be assumed that gout occurs only in men, particularly those in the older age range, who are obese and use sufficient alcohol to have a red nose, or in those who are plethoric, or in individuals of wealth who can afford the help of servants. Actually, the only true characteristics of gout are that it affects the extremities and that it causes great redness, swelling and pain.

The exhibit is divided into three parts: (1) results of a study of the basic clinical features in 450 patients with gout personally seen prior to 1949; (2) the problem of the diagnosis of gout, stressing the importance of its classical clinical course, the common finding of a normal serum uric acid value during or soon after an attack of gout and the roentgenologic manifestations in cases of gout; (3) therapy, covering first the available methods for combating acute attacks and, second, the effective methods for carrying out interval therapy aimed at complete control of gout. The important role of BENEMID® in maintenance treatment is indicated.

Adapted from a diagnostic clinic presented at the thirty-eighth annual Assembly of the Interstate Postgraduate Medical Association at Chicago and an exhibit presented at the 1953 Annual Meeting of the American Medical Association, New York City.

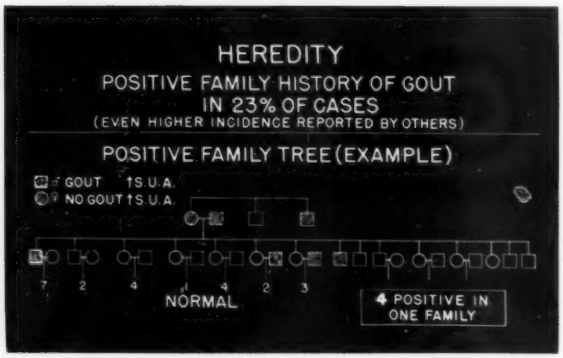
The author wishes to acknowledge the assistance of Dr. Francis G. Barnum, Jr., former Fellow in Internal Medicine, The Lahey Clinic, in correlating the data regarding the clinical features of gout.

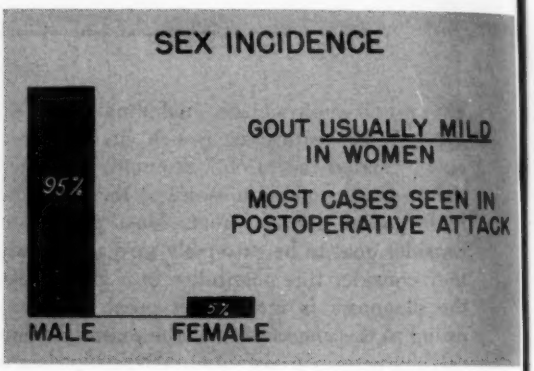
CLINICAL FEATURES

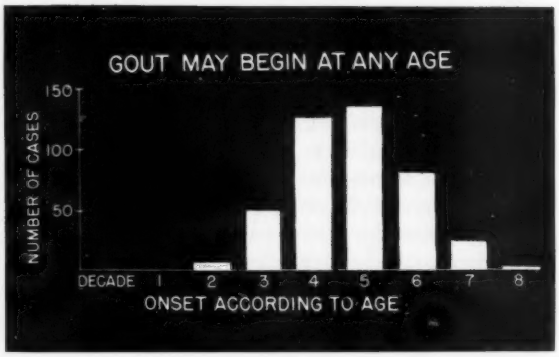
REVIEW OF 450 CASES (1935 — 1949)

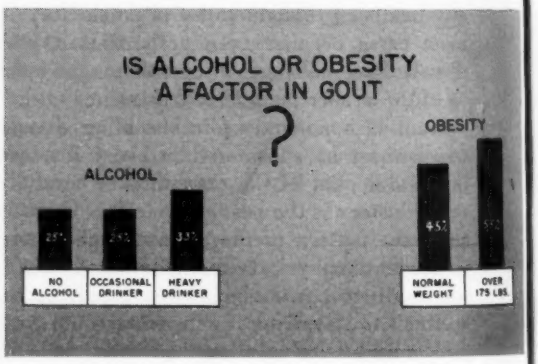
RACE

Gout is more common among patients of Italian descent. Twelve per cent of cases were Italian patients. Why? Other nationalities were evenly affected—0.5 to 1 per cent.



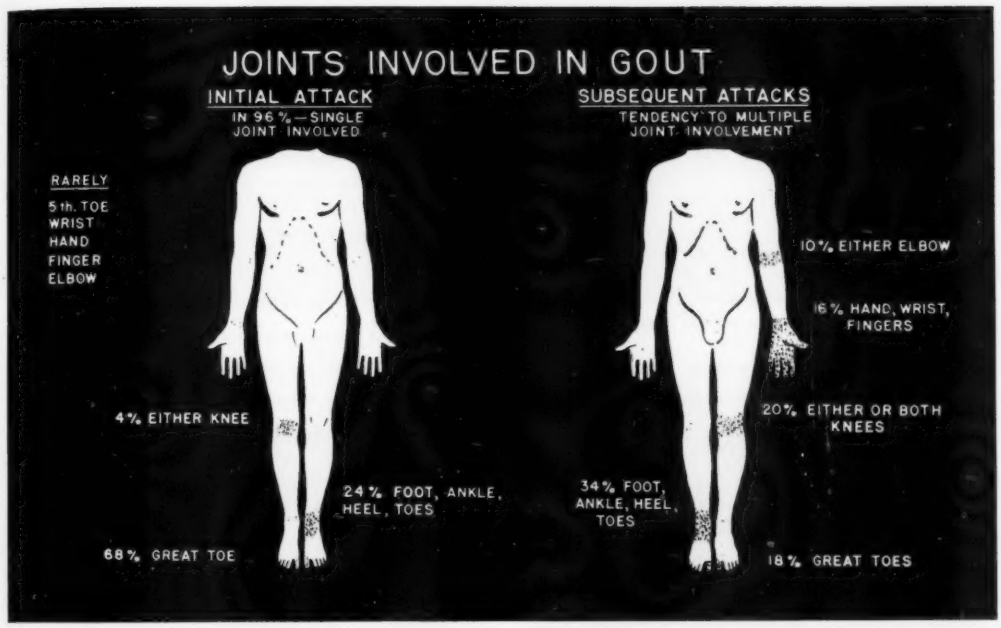






PRECIPITATING CAUSES OF ACUTE GOUT

A. Trauma
   Major
   Minor
B. Operation
C. Weight reducing diet
D. High fat (ulcer) diet
E. Infections
F. Excess alcohol
G. Excess food
H. Nervous fatigue
I. Idiopathic



DURATION OF FIRST GOUT ATTACK

	Percentage
1 day to 2 weeks	66
1 day to 1 month	86
Longest attack was 5 months	

INTERVAL BETWEEN FIRST AND SECOND ATTACKS

(varies from 1 month to 27 years)

	Percentage
1 to 5 months	16
6 to 8 months	20
1 year	40
1 to 5 years	16

SUBSEQUENT ATTACKS

	Percentage
Interval	
Within 1 to 5 months	40
Within 6 to 12 months	50
Duration	
1 day to 1 month	70

Previous diagnosis of gout was made in only 53 per cent of cases.
Physicians tend to avoid the diagnosis of gout.

TREATMENT WHEN PREVIOUSLY DIAGNOSED

	Percentage
Diet (low purine)	16
ATOPHAN®	27
Colchicine	65
Alcohol was rarely restricted	

TOPHI

(present in 21 per cent of cases)

	Percentage
In ears alone	43
Ears negative (tophi elsewhere)	15
Multiple sites	30
Patients with tophi who had gout more than 6 years	88
Patients who had no tophi but had gout more than 15 years	50

X-RAY FINDINGS

	Percentage
Compatible with gout	15
Negative	20
Degenerative arthritis	36
Hallux valgus	11
Soft tissue swelling	11
Also considered: rheumatoid arthritis and sarcoidosis	
X-ray changes in patients with gout for only 2 years (? gout)	17
Negative x-ray findings in patients with gout for more than 10 years	18

COINCIDENTAL DISEASES

	Percentage
Common	
Obesity	23
Hypertension	9
Coronary heart disease	9
Less common	
Degenerative arthritis	
Gallstones	
Nephritis	
Hypertrophied prostate	
Kidney stones	3
Diabetes mellitus	1.3

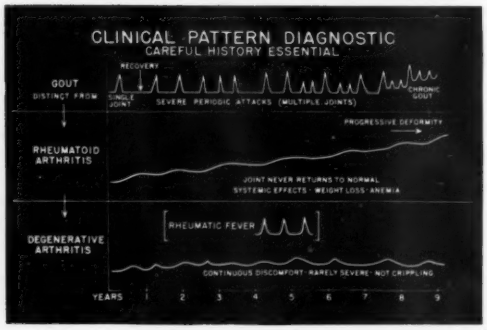
DIAGNOSIS

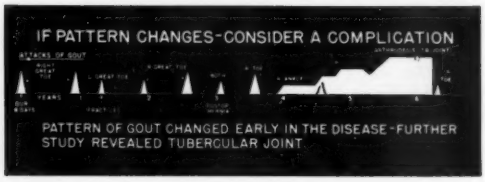
GOUT IS NOT UNCOMMON
SHOULD BE CONSIDERED IN EVERY CASE INVOLVING A PAINFUL JOINT OF THE EXTREMITIES

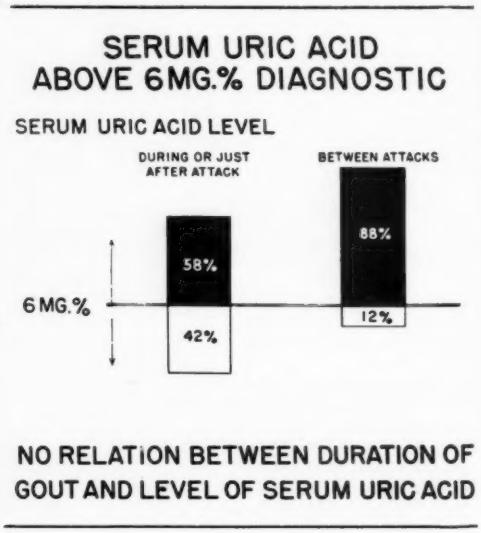
DIAGNOSIS MUST DEPEND CHIEFLY ON THE HISTORY

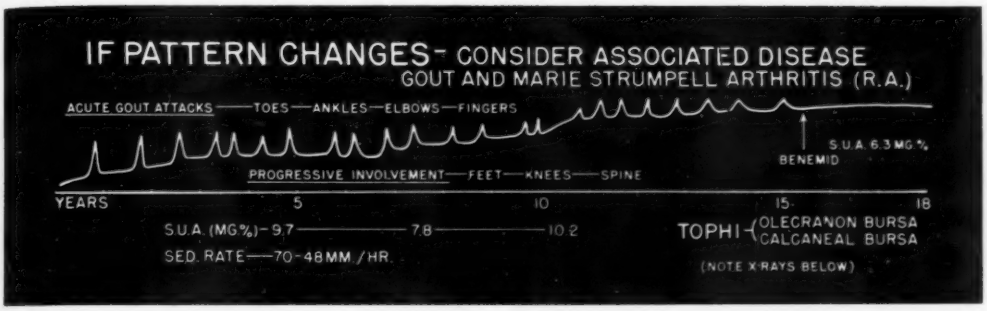
A. No characteristic physical habitus found in gout
B. Mode of living is not a factor
C. Serum uric acid may be normal (especially during attack)
D. X-rays of involved joint may be negative even late in the disease
E. Tophi—late manifestation (or absent)
F. Joint may be normal at examination
G. Great toe (diagnostic joint) not always involved
H. Positive family history may confirm the diagnosis of gout

THESE TYPES OF SHOES IN THE ABSENCE OF SEVERE TRAUMA MAKE THE DIAGNOSIS




IF PATTERN CHANGES - CONSIDER A COMPLICATION
PATTERN OF GOUT CHANGED EARLY IN THE DISEASE - FURTHER STUDY REVEALED TUBERCULAR JOINT





Large tophi; prepatellar bursa; yellow plaques present.

Tophi of ear—must be searched for. Roll back ear.

Extremely large tophi of fingers; gout for 27 years.

Tophi of olecranon bursa. Yellow plaques present.

Draining tophi of toes, both great and right third toe.

Tophus of calcaneal bursa. Great toe is also involved.

X-RAY CHANGES IN GOUT

EARLY CHANGES

a. Cystlike areas in left metatarsal head and base of proximal phalanx; *(right)* normal.

b. Loss of medial corners at base of proximal phalanx. Lateral view shows loss of corners.

PROGRESSIVE BONE CHANGES

1937

1946

Radiolucence of first metatarsal head and hallux valgus increased (1946).

TOPHUS FORMATION

a. Tophus with calcification. Destruction of superior angle base of proximal phalanx.

b. Olecranon bursa with slight calcification.

ADVANCED BONE CHANGES

a. Extensive changes—large cystlike area of proximal phalanx of great toe (gout for two and a half years).

b. Extensive destruction of bones. Note terminus of first phalanx of great toe.

COMBINED ARTHRITIS—GOUT AND MARIE-STRUMPELL DISEASE

Spine—calcification of anterior longitudinal ligament.

Foot—destructive changes of gout (great toe). Bony spurring of peripheral Marie-Strümpell arthritis.

March 1954

THERAPY

NO CURE BUT CONTROLLABLE

TREATMENT OF ACUTE GOUT

Oral Colchicine

Best home treatment: 1/120 gr. hourly for 6 to 8 doses. Repeat in 48 hours if needed.

20 per cent glucose, 500 cc. twice daily, intravenously. Useful in postoperative gout where colchicine is contraindicated.

ORAL CORTISONE
- 10 cases treated
- Dose: 100 mg. daily
- Results: Unsatisfactory

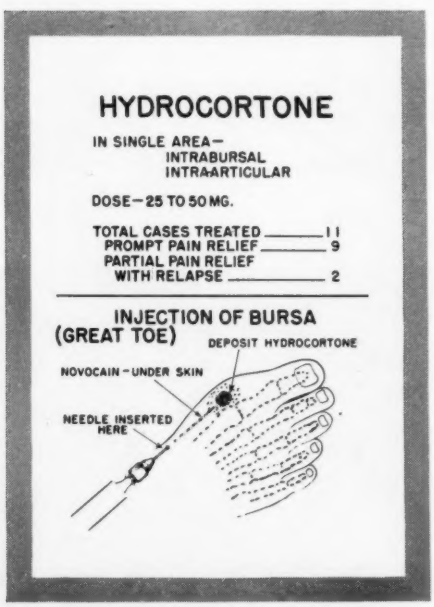
CORTISONE, INTRAMUSCULARLY
- Results: Unsatisfactory

ACTH, INTRAMUSCULARLY
- 13 cases treated
- Dose: 25 to 50 mg.
- Results: Unpredictable unless given every 4 to 6 hours

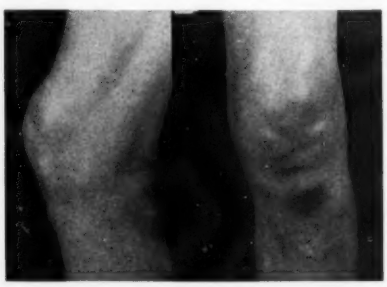
ACTH, INTRAVENOUSLY
- 29 patients treated
- 500 cc. of 5 per cent glucose
- 25 to 50 mg. ACTH
- Slow drip for 5 to 6 hours
- Single treatment in acute cases; multiple treatment in prolonged attacks
- Dramatic relief in most cases in 4 to 6 hours
- No failures

AVAILABLE MEDICATIONS
- *A. Oral colchicine
- B. ACTH
  - 1. Intramuscular injection
  - *2. Slow drip, intravenous injection
- *C. ACTHAR® gel
- *D. HYDROCORTONE®
- E. 20 per cent glucose
- F. Cortisone

Not used in this study:
Colchicine, intravenously
BUTAZOLIDIN®



Acthar gel, intramuscularly—successful in 8 cases.



Before therapy (100 units)—painful flexion deformity.

24 hours later—painless, straight; daily colchicine for one week.

MAINTENANCE OR INTERVAL TREATMENT

RESULTS OF STRICT DIET AND SALICYLATES

Most effective in early gout
Eliminates major attacks
Restores serum uric acid to normal

Partially helpful in late gout
Fewer major attacks
Serum uric acid reduced—not to normal

ESSENTIALS OF BENEMID TREATMENT

1. Start with large doses—2 to 3 gm.; reduce doses as serum uric acid falls.
2. Maintenance dose must be individualized.
3. Colchicine must be given with Benemid during first three months of treatment to prevent recurring gout.

*Reactions to Benemid (3 in 80 cases)

Fever and skin	1
Headache	1
Nausea	1

CONTROL POSSIBLE

By Continuous Individualized Therapy

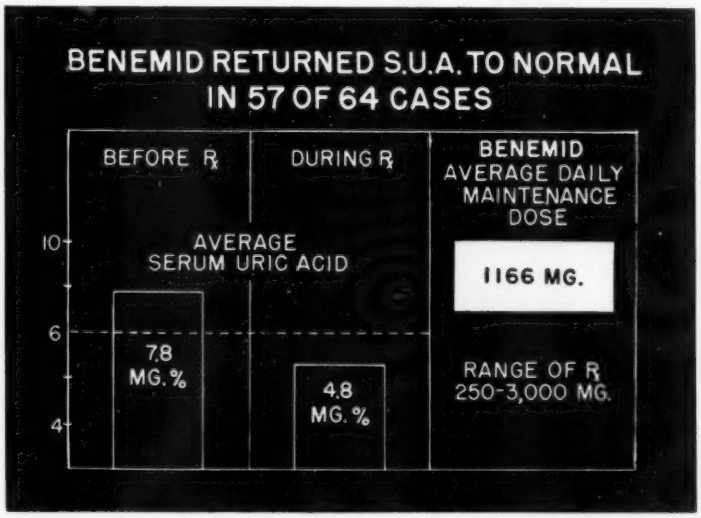
A. Low purine—low fat diet plus salicylates and no alcohol.

B. Low purine—low fat diet plus Benemid.

C. Benemid without diet restriction.

D. Butazolidin, *only* if Benemid sensitive (high reaction incidence with Butazolidin).

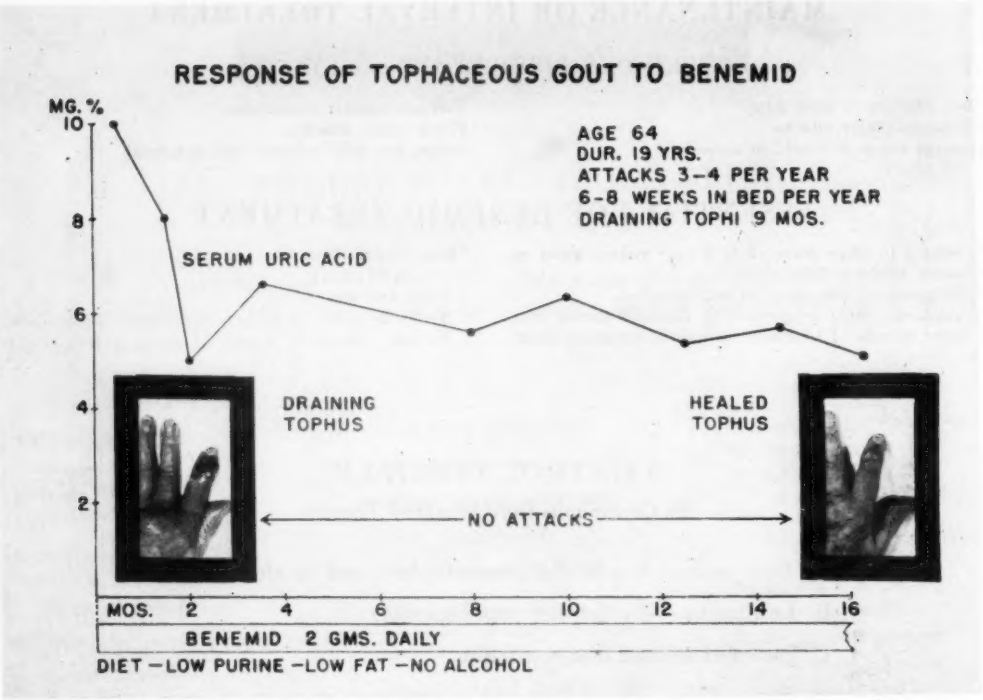
In resistant cases, use periodic injections of Acthar gel.

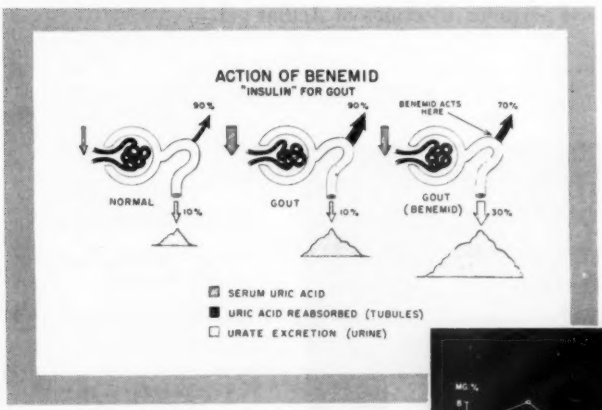


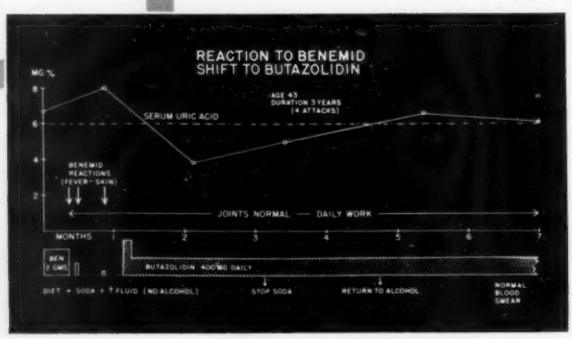
RESULTS OF BENEMID THERAPY

(64 cases followed for 3 to 24 months)

Normal S.U.A.; no attack	40
Normal S.U.A.; occasional attack (Attacks early in therapy; 11 cases with no added colchicine)	16
Normal S.U.A.; severe attacks	1
Elevated S.U.A. in spite of Benemid	7
Fewer attacks	4
Continued attacks	3


RESPONSE OF TOPHACEOUS GOUT TO BENEMID
MG. %
10
8
6
4
2
AGE 64
DUR. 19 YRS.
ATTACKS 3–4 PER YEAR
6–8 WEEKS IN BED PER YEAR
DRAINING TOPHI 9 MOS.
SERUM URIC ACID
DRAINING TOPHUS
HEALED TOPHUS
NO ATTACKS
MOS. 2 4 6 8 10 12 14 16
BENEMID 2 GMS. DAILY
DIET – LOW PURINE – LOW FAT – NO ALCOHOL


ACTION OF BENEMID
"INSULIN" FOR GOUT
90%
90%
BENEMID ACTS HERE
70%
NORMAL
10%
GOUT
10%
GOUT (BENEMID)
30%
SERUM URIC ACID
URIC ACID REABSORBED (TUBULES)
URATE EXCRETION (URINE)


REACTION TO BENEMID
SHIFT TO BUTAZOLIDIN
MG. %
AGE 43
DURATION 3 YEARS
(4 ATTACKS)
SERUM URIC ACID
BENEMID REACTIONS (FEVER - SKIN)
JOINTS NORMAL — DAILY WORK
MONTHS
BUTAZOLIDIN 400 MG DAILY
DIET + SODA + FLUID (NO ALCOHOL)
STOP SODA
RETURN TO ALCOHOL
NORMAL BLOOD SMEAR

GENERAL PRACTICE *Review*

This department offers the latest, proved methods for the treatment and management of commonly encountered conditions based on the extensive experience of the physicians who prepare these summaries for POSTGRADUATE MEDICINE.

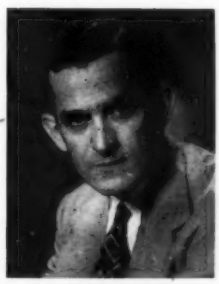
Rehabilitation of Patients with Heart Disease

HERMAN K. HELLERSTEIN AND ELAINE GOLDSTON*

Western Reserve University School of Medicine, Cleveland

THE purpose of this report is to describe the process of rehabilitation of the patient with heart disease from the initial illness through the convalescent period to the return to the world of work. The active work of the physician as a guiding force and cohesive influence throughout rehabilitation will be described in detail.

Rehabilitation of the patient with heart disease involves the same basic principles and problems as the rehabilitation of patients with any type of disease, physical or mental. The term rehabilitation is defined as a process by which a patient is returned realistically to his greatest physical, mental, social, vocational and economic usefulness, and, if employable, is provided an opportunity for gainful employment in a competitive industrial world.[1] Successful rehabilitation, in this modern sense, is not restricted to economic or vocational rehabilitation alone; rather it is the complete development of a pattern of living which will enable the patient to enjoy to the fullest his physical and mental capacities with due allowances for his disabilities.



HERMAN K. HELLERSTEIN

ELAINE GOLDSTON

Rehabilitation of patients with heart disease has become a problem of increasing significance as our population pattern has been skewed toward the older age groups. As a result there is an absolute increase of the aging population and *pari passu*, more vascular disease. The growing incidence of cardiovascular disease in private practice and in hospital practice has been well established. Today cardiovascular disease is one of the most important causes of disability and death.

*Department of Medicine, School of Medicine, Western Reserve University; University Hospitals of Cleveland and the Work Classification Clinic of the Cleveland Area Heart Society, Cleveland, Ohio.

Thus approximately 10 million persons are handicapped by diseases of the cardiovascular system. Absenteeism due to cardiovascular disease in the first six months of 1952 was exceeded only by the absenteeism due to respiratory diseases.[2]

The process of rehabilitation is considered to begin at the moment the patient is first stricken with the disease or at least at the time when he is over the acute illness to the point of being free of pain and out of the life-endangering stage. The need for rehabilitation is considered to exist in all etiologic groups, including rheumatic, degenerative heart disease (arteriosclerotic heart disease, hypertensive cardiovascular disease), cor pulmonale, iatrogenic heart disease, congenital heart disease and syphilis. Patients in all economic groups can benefit from a program of rehabilitation. Even though the disease process may be relatively unstable, all patients are eligible for rehabilitation, although not necessarily for retraining.[1]

The goals of rehabilitation are variable and depend on the stage and severity of the disease process. While the long-term goal is eventual restoration of the patient to a gainful productive life, there are interim goals; the transitions from hospital to home to the outside social and work world (figure 1). For some patients the world of work means business and industry, to others, housework or professions. There is a definite relationship between the ultimate goal in the individual case and the disease process. Retraining, for example, would not be considered advisable for the patient in whom the retraining process is slower than the course of the disease.[1] Each patient, however, is eligible for rehabilitation to his maximum attainment. The rate and goals of rehabilitation must be individualized and must be commensurate with the emotional and physical improvement of the patient. Furthermore, the process of rehabilitation may be modified by the introduction of new types of therapy and by changes in the patient's response to medical therapy.

Total Evaluation of the Patient by the Team Approach

Because the process of total evaluation of a person with heart disease is complex, a team approach is necessary in order to concentrate the knowledge of multiple disciplines and to integrate them in the individual case. The responsible physician is the guiding force and provides a cohesive influence since the basic problem is essentially that of a person with heart disease. The various disciplines that are integrated during the course of rehabilitation include medical, psychiatric, social service, occupational therapy, occasionally physiotherapy, vocational counseling, prevocational training and sheltered workshops.

The *modus operandi* of the team approach has been developed and described elsewhere.[3] In a true team approach the various members of the team have equal status and their contributions are considered to have relatively equal significance. There is bound to be over-

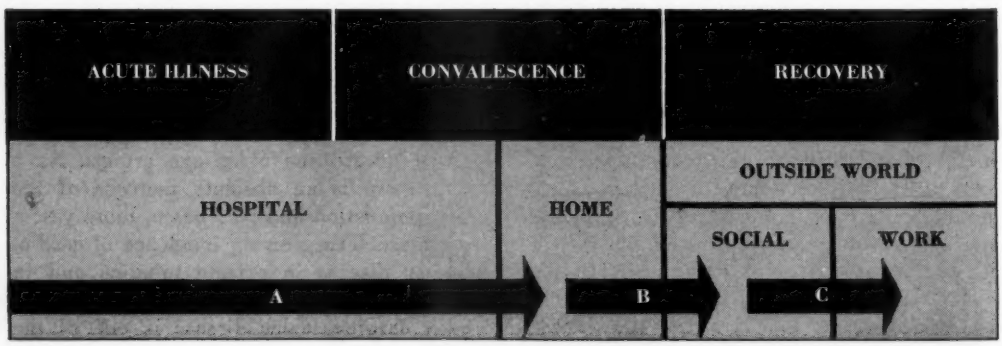
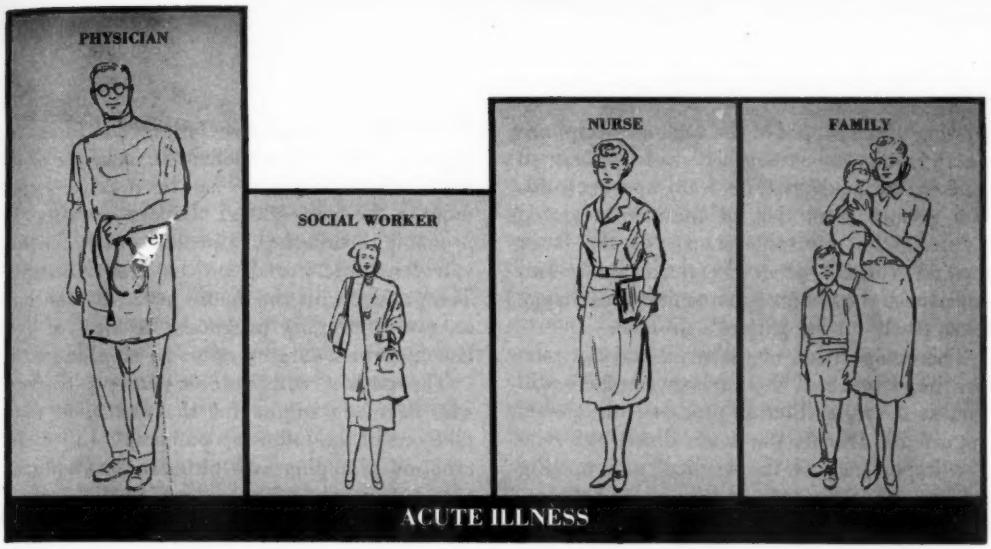


FIGURE 1.



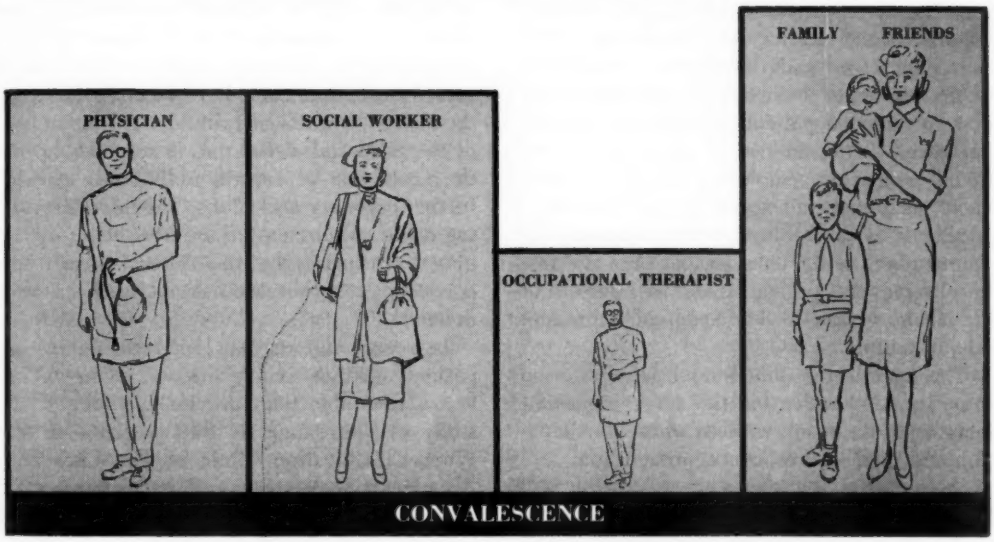
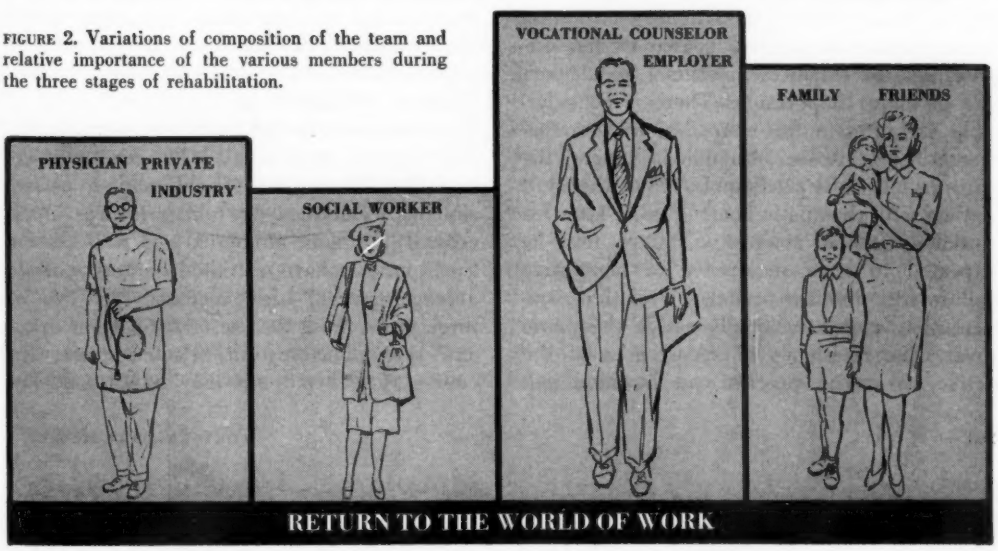


FIGURE 2. Variations of composition of the team and relative importance of the various members during the three stages of rehabilitation.



lapping of the scopes of the various disciplines which tends to strengthen rather than to weaken the analysis. The team approach differs greatly from that of the nonintegrated method (the referral system). In the latter method various observers make their own analyses and have no opportunity to exchange ideas freely on the patient's problem.

The composition of the team and the relative importance of the various members will vary as the rehabilitation process is developed (figure 2). During the acute illness the relative importance of the medical and nursing professions is greatest, and the role of the occupational therapist and social worker is secondary. During the convalescent period the importance of support offered by family, friends, social service and vocational counseling increases and the relative importance of the physician decreases. In the final phase of returning the patient to work life, the importance of the industrial physician, vocational counselor, employer, selective placement personnel and social service increases. Ideally it is desirable to have continuity of the members of the team so that they are able to observe the patient from the period of the acute illness to his eventual successful rehabilitation.

Throughout the illness and rehabilitation program, the patient is the most important member of the team, without whose participation and interest the team approach fails.

Important Factors in Rehabilitation

Nature and course of heart disease—The type of heart disease, the extent of structural involvement, the natural course of the disease, and the extent of functional impairment are of major importance. There is considerable variation in the course of a given patient's heart disease, although in general the prognosis is quite predictable.[5] Thus the adult patient with rheumatic heart disease, after his initial episode of congestive failure, may be expected to have recurrence of congestive failure with interim periods of relative compensation, and occasionally active rheumatic fever. The frequency of recurrences of the active rheumatic process can be modified. Treatment of congestive failure continues to improve. Thromboembolism in patients with mitral valvular disease has been fairly common in the past and at the present time is probably decreasing, especially after mitral valvular surgery and anticoagulant therapy. The patient with rheumatic heart disease has an ever-improving prognosis because of the benefits which surgery offers in eligible cases.

The patient with coronary artery disease who develops angina for the first time may take one of the following pathways: (1) exacerbation of angina with ultimate development of coronary occlusion and myocardial infarction, (2) abatement, spontaneous or otherwise, of the angina and (3) later recurrence of angina with or without subsequent acute coronary thrombosis. A dual process of narrowing of the coronary arteries and collateral vessel formation occurs at variable rates in the hearts of practically all adults. Dominance of the collateral circulation is responsible for the protection of certain individuals against further coronary occlusions. The factors favoring collateral circulation are now being determined. Surprisingly, the natural course of coronary artery disease has not yet been well defined.

In recent reports the long-term course of patients with coronary disease seems to be less unfavorable than previously thought.[4] A study of approximately 500 patients of the Work Classification Clinic of The Cleveland Area Heart Society revealed that patients with coronary artery disease improve twice as frequently as they deteriorate over a three year period of observation. Lindgren found spontaneous improvement in 27 per cent of patients with more severe coronary arteriosclerosis.[6] Similarly the long-term course of hypertensive patients varies.[7] In females diastolic hypertension is much less ominous than in males. The course of malignant hypertension with sustained diastolic pressures in excess of 120 mm. of mercury is well known. Such patients have a limited outlook with an average general life expectancy of two or three years. With the use of antipressor drugs and sympathectomy in selected cases, the course of such patients may be altered. The

outlook of patients with milder degrees of hypertension is much more favorable.[7]

Emotional factors—In 46 per cent of the patients studied at the Cleveland Work Classification Clinic, emotional factors were next in importance to the heart disease per se. Much of this emotional difficulty was based on fear, anxiety and tension states which developed in previously susceptible individuals. Even in the most stable patients the onset of heart disease is associated with a short period of anxiety and depression. This usually passes, and a satisfactory adjustment is made. The pre-illness personality and temperament, particularly in patients with a "vascular-coronary constellation," are contributing factors. In such aggressive patients the impact of illness may cause a prolonged period of anxiety, fits of depression, and complaints referable to other systems. When a patient with heart disease is informed that he has heart disease, the foundations of his normal existence are literally threatened. The fear of death leaves him helpless and unable to work. Frequently he is overwhelmed by the fear of disability or sudden death. In many instances, newspaper publicity devoted to heart disease (obituary columns, heart campaigns) may be responsible for unfounded fears. Later, emotional problems are exaggerated by economic and social pressures, loss of income, financial responsibilities, indebtedness, mortgages, the burden of a family of growing children, and by the need to maintain a certain standard of living. Over-reaction of the family to the patient and his reaction to the illness is also contributory.

Most important, however, is iatrogenic disability so often produced unwittingly. This iatrogenic disability may stem from simple misstatements, or misinterpretation by the patient of the physician's casual comments, ominous shaking of the head, careless statements by the physician such as "this is the largest heart," "loudest murmur," or "the most beautiful heart attack I have ever seen," etc., or by the physician who imposes needless unreasonable restrictions on the patient because of overinterpretation or misinterpretation of murmurs, thrills, electrocardiogram and x-ray findings. In such instances the physician loses sight of the fact that there is not a close correlation between the electrocardiogram at rest and the functional capacity of the cardiovascular system. Much iatrogenic disability is produced by the transfer of the physician's own insecurity and anxiety to the patient. The patient readily senses the uneasiness which often subtly overtakes many physicians in the treatment of the seriously ill cardiac. A smiling face and a hopeful cheerful attitude of the physician during the examination and subsequent visits have therapeutic and prophylactic value, especially when based on the improved outlook of modern therapy.

Vocational factors include such features as age, race, previous training, literacy, educational background, work history and work performance, vocational interest in hobbies, skill levels and job opportunities. The problem of transportation may be of prime importance. The stresses of traveling to and from a job, and the work load imposed by walking to the locker room or place of employment may far exceed the expenditure of energy required to perform the job. Taxing features on the job such as dust, noise, lifting and incentive production, in selected instances, may be most important in determining the employability of a person with heart disease. Misuse of pre-employment examination and rigid administration of seniority rules are often stumbling blocks in total rehabilitation. Pension plans and insurance disability payments also modify the need and the rate of rehabilitation. In their absence the urgency of rehabilitation becomes even greater.

Other diseases of significance, such as obesity, diabetes mellitus, peptic ulcer, gallbladder disease, tuberculosis, arteriosclerosis of other organs, particularly the brain, the extremities and kidneys, neoplasm and progeria are examples which may complicate rehabilitation and prognosis.

The success of rehabilitation depends on the severity of the heart disease, the management during the acute illness and the convalescent period and the work adjustment phase, the emotional complications, and selective placement in industry or business.

Management at Onset and During the Acute Illness

In the subsequent discussion it is assumed that adequate medical therapy is prescribed in all instances. The importance of rest, relief of pain, restoration of the oxygen system, adequate nutrition and sedation is taken for granted. Specific therapeutic and rehabilitative measures must be planned in detail to fit the specific needs of the patient.

During the treatment of acute episode—It is important that the physician's concern over the prospect of each case not be transferred to the patient. A positive, realistically hopeful attitude of the physician is required and is warranted by the statistical facts that 85 per cent of patients do survive an acute episode of myocardial infarction,[8] most patients recover from acute pulmonary edema and congestive failure, and the incidence, mortality and morbidity of acute rheumatic fever have improved considerably under the regimen of bed rest, antibiotics, ACTH, cortisone and salicylates. The importance of avoiding the transfer of the physician's anxiety to the patient cannot be overstressed.

Unknowingly severe emotional trauma is often produced by casual remarks by the nurses and house staff, and by learned discussion of prognosis in the patient's presence, especially when he is thought to be heavily sedated. During the period of acute illness, excessive restriction of the patient, prolonged narcosedation and prolonged unnecessary use of oxygen (especially if its use is not explained briefly to the patient as being therapeutic in the same fashion that digitalis and other medications are used) are some of the obvious but generally unappreciated methods of producing needless fears.

In summary, during the treatment of the acute episode it is important that the physician present a positive attitude which is hopeful and realistic, based on the knowledge that most patients recover from acute episodes of myocardial infarction, pulmonary edema and congestive failure.

After the acute crisis is over—There is a need to explain the immediate and long-term goals to the patient and his family. The patient will need help in accepting the fact of his heart disease. The patient should be informed in general terms of the plan of therapy, especially during the time of hospitalization and during convalescence. A concerted effort should be made to help the patient develop some insight into his disease and to encourage a receptive mood for future rehabilitation. From the very beginning a positive attitude must be maintained that the patient will eventually return to the competitive world successfully. Emphasis should be placed on the high recovery rate of patients with heart disease in general and of the excellent vocational readjustment which is now based on factual observations. In addition, the improvement in prognosis and therapy can be brought to the patient's attention indirectly.

If the patient has congestive failure, the regimen of dietary control, cardiac medication and action of diuretics should be presented to the patient in general physiologic terms. A simple description of heart function is well within the grasp of most patients. If the patient is hypertensive and obese, and weight reduction will be required, the general principles and importance of weight reduction should be presented.

If the patient has coronary artery disease, the concept of collateral circulation should be presented. Implanting and fostering the concept of collateral circulation has positive psychotherapeutic affects. In our opinion, the unfortunate analogy that arteriosclerosis is "like rust accumulating in pipes" is taboo, since the concomitant development of collateral circulation is ignored. Naturally, if the patient is told that he has had a coronary occlusion he may be overwhelmed by the anxiety that is associated with the term. He easily becomes depressed and fatalistically but reluctantly accepts the idea that his productive days are over. Unfortunately this can be confirmed in the patient's mind by admonitions from the physician that it is going to be necessary for him to change his "whole way of living." Nothing need be further from the truth. It will be stated later that 76 per cent of patients return to the same vocational and occupational classification.

Hospital Convalescence

Up to this moment the medical care has predominated in the management of the patient. During this period (which usually starts on the third to fifth day after admission, occasionally sooner, and ends approximately after three or four weeks in the hospital) the coverage and management of the patient differs. Here the team is organized and the team approach is put into action.

From the medical standpoint rehabilitation takes many forms. It is quite reassuring to the patient to be allowed use of a bedside commode and later, when he can walk safely, to be allowed use of the bathroom if it is no more than 10 or 15 feet away from the bed. Benton and associates have demonstrated that less energy is expended in using a bedside commode than in using a bedpan.[9] The value of the bedside chair in the treatment of myocardial infarction and congestive failure has been amply demonstrated by Levine.[10] Not only is it beneficial from the circulatory standpoint, but psychologically it removes the patient from the realm of complete bed restriction to that of relative liberty. Bedfast invalidism is prevented by such management. The patient is happier since the days seem considerably shorter in the hospital when he is able to sit comfortably several hours in a bedside chair.

In addition, medical management should be concerned with the prevention of the ill effects of excessive bed rest. During World War II, Keys and others demonstrated that excessively restrictive bed rest was associated with certain definite catabolic changes, loss of nitrogen, phosphorus, calcium, muscular wasting, decrease in skeletal muscle tone, bone atrophy, vasomotor instability, and decrease in cardiac output, blood volume, blood pressure, heart size and exercise tolerance.[11,12] Healthy normal young soldiers required from two to six weeks to recover their tolerance to moderate exercise. Many such healthy subjects restricted to bed for a period of several weeks manifested signs of neurocirculatory asthenia on resuming physical activity, i.e., a relatively rapid heart rate, a feeling of faintness and dizziness, weakness, asthenia and anxiety. Several days before ambulation, the patient should be instructed to exercise his legs by bending his knees and flexing and extending his ankles several times an hour. Patients with heart disease who have been excessively restricted may also suffer the ill effects of bed rest. It is important and reassuring to inform the patient of the normalcy of this response to early ambulation.

The patient should be encouraged to participate *actively* in his own rehabilitation. During his acute illness, necessarily he has "to renounce ownership" of his own body and permit it to be handled passively. He is dressed and undressed, fed, cleaned, washed, helped with urination and defecation, turned from one side to the other, his nakedness exposed to nurse and doctor, regardless of sex, of decencies and of conventional restrictions. He is, as it were, under orders subjected to a hygienic routine which implies a major disregard for his personal attitude and preferences. Characteristically enough, many adults sum up this experience as being "treated as a baby," or as "a complete return to conditions of their childhood."[13] This period of passivity should be abbreviated as much and as soon as possible. For the coronary and hypertensive patients enforced passivity is especially harmful, being the antithesis of their aggressive and dynamic personalities.

An educational program should be instituted at this time from other standpoints. If some form of dietary restriction is advisable the general philosophy of dietary control should be presented. The dietitian should have an opportunity to discuss special diets leisurely during several interviews with the patient and his wife. It should be made clear to the patient and his wife that a restricted diet does not mean a tasteless diet.[14] Great emphasis and care should be placed on preparing diets which are attractive as well as therapeutic. The physician should make available to the patient selected articles dealing with the adjustment of other patients to their heart disease. Such lay reading should be individualized. Care should be taken to avoid several publications now in print which empha-

lapping of the scopes of the various disciplines which tends to strengthen rather than to weaken the analysis. The team approach differs greatly from that of the nonintegrated method (the referral system). In the latter method various observers make their own analyses and have no opportunity to exchange ideas freely on the patient's problem.

The composition of the team and the relative importance of the various members will vary as the rehabilitation process is developed (figure 2). During the acute illness the relative importance of the medical and nursing professions is greatest, and the role of the occupational therapist and social worker is secondary. During the convalescent period the importance of support offered by family, friends, social service and vocational counseling increases and the relative importance of the physician decreases. In the final phase of returning the patient to work life, the importance of the industrial physician, vocational counselor, employer, selective placement personnel and social service increases. Ideally it is desirable to have continuity of the members of the team so that they are able to observe the patient from the period of the acute illness to his eventual successful rehabilitation.

Throughout the illness and rehabilitation program, the patient is the most important member of the team, without whose participation and interest the team approach fails.

Important Factors in Rehabilitation

Nature and course of heart disease—The type of heart disease, the extent of structural involvement, the natural course of the disease, and the extent of functional impairment are of major importance. There is considerable variation in the course of a given patient's heart disease, although in general the prognosis is quite predictable.[5] Thus the adult patient with rheumatic heart disease, after his initial episode of congestive failure, may be expected to have recurrence of congestive failure with interim periods of relative compensation, and occasionally active rheumatic fever. The frequency of recurrences of the active rheumatic process can be modified. Treatment of congestive failure continues to improve. Thromboembolism in patients with mitral valvular disease has been fairly common in the past and at the present time is probably decreasing, especially after mitral valvular surgery and anticoagulant therapy. The patient with rheumatic heart disease has an ever-improving prognosis because of the benefits which surgery offers in eligible cases.

The patient with coronary artery disease who develops angina for the first time may take one of the following pathways: (1) exacerbation of angina with ultimate development of coronary occlusion and myocardial infarction, (2) abatement, spontaneous or otherwise, of the angina and (3) later recurrence of angina with or without subsequent acute coronary thrombosis. A dual process of narrowing of the coronary arteries and collateral vessel formation occurs at variable rates in the hearts of practically all adults. Dominance of the collateral circulation is responsible for the protection of certain individuals against further coronary occlusions. The factors favoring collateral circulation are now being determined. Surprisingly, the natural course of coronary artery disease has not yet been well defined.

In recent reports the long-term course of patients with coronary disease seems to be less unfavorable than previously thought.[4] A study of approximately 500 patients of the Work Classification Clinic of The Cleveland Area Heart Society revealed that patients with coronary artery disease improve twice as frequently as they deteriorate over a three year period of observation. Lindgren found spontaneous improvement in 27 per cent of patients with more severe coronary arteriosclerosis.[6] Similarly the long-term course of hypertensive patients varies.[7] In females diastolic hypertension is much less ominous than in males. The course of malignant hypertension with sustained diastolic pressures in excess of 120 mm. of mercury is well known. Such patients have a limited outlook with an average general life expectancy of two or three years. With the use of antipressor drugs and sympathectomy in selected cases, the course of such patients may be altered. The

outlook of patients with milder degrees of hypertension is much more favorable.[7]

Emotional factors—In 46 per cent of the patients studied at the Cleveland Work Classification Clinic, emotional factors were next in importance to the heart disease per se. Much of this emotional difficulty was based on fear, anxiety and tension states which developed in previously susceptible individuals. Even in the most stable patients the onset of heart disease is associated with a short period of anxiety and depression. This usually passes, and a satisfactory adjustment is made. The pre-illness personality and temperament, particularly in patients with a "vascular-coronary constellation," are contributing factors. In such aggressive patients the impact of illness may cause a prolonged period of anxiety, fits of depression, and complaints referable to other systems. When a patient with heart disease is informed that he has heart disease, the foundations of his normal existence are literally threatened. The fear of death leaves him helpless and unable to work. Frequently he is overwhelmed by the fear of disability or sudden death. In many instances, newspaper publicity devoted to heart disease (obituary columns, heart campaigns) may be responsible for unfounded fears. Later, emotional problems are exaggerated by economic and social pressures, loss of income, financial responsibilities, indebtedness, mortgages, the burden of a family of growing children, and by the need to maintain a certain standard of living. Over-reaction of the family to the patient and his reaction to the illness is also contributory.

Most important, however, is iatrogenic disability so often produced unwittingly. This iatrogenic disability may stem from simple misstatements, or misinterpretation by the patient of the physician's casual comments, ominous shaking of the head, careless statements by the physician such as "this is the largest heart," "loudest murmur," or "the most beautiful heart attack I have ever seen," etc., or by the physician who imposes needless unreasonable restrictions on the patient because of overinterpretation or misinterpretation of murmurs, thrills, electrocardiogram and x-ray findings. In such instances the physician loses sight of the fact that there is not a close correlation between the electrocardiogram at rest and the functional capacity of the cardiovascular system. Much iatrogenic disability is produced by the transfer of the physician's own insecurity and anxiety to the patient. The patient readily senses the uneasiness which often subtly overtakes many physicians in the treatment of the seriously ill cardiac. A smiling face and a hopeful cheerful attitude of the physician during the examination and subsequent visits have therapeutic and prophylactic value, especially when based on the improved outlook of modern therapy.

Vocational factors include such features as age, race, previous training, literacy, educational background, work history and work performance, vocational interest in hobbies, skill levels and job opportunities. The problem of transportation may be of prime importance. The stresses of traveling to and from a job, and the work load imposed by walking to the locker room or place of employment may far exceed the expenditure of energy required to perform the job. Taxing features on the job such as dust, noise, lifting and incentive production, in selected instances, may be most important in determining the employability of a person with heart disease. Misuse of pre-employment examination and rigid administration of seniority rules are often stumbling blocks in total rehabilitation. Pension plans and insurance disability payments also modify the need and the rate of rehabilitation. In their absence the urgency of rehabilitation becomes even greater.

Other diseases of significance, such as obesity, diabetes mellitus, peptic ulcer, gallbladder disease, tuberculosis, arteriosclerosis of other organs, particularly the brain, the extremities and kidneys, neoplasm and progeria are examples which may complicate rehabilitation and prognosis.

The success of rehabilitation depends on the severity of the heart disease, the management during the acute illness and the convalescent period and the work adjustment phase, the emotional complications, and selective placement in industry or business.

Management at Onset and During the Acute Illness

In the subsequent discussion it is assumed that adequate medical therapy is prescribed in all instances. The importance of rest, relief of pain, restoration of the oxygen system, adequate nutrition and sedation is taken for granted. Specific therapeutic and rehabilitative measures must be planned in detail to fit the specific needs of the patient.

During the treatment of acute episode—It is important that the physician's concern over the prospect of each case not be transferred to the patient. A positive, realistically hopeful attitude of the physician is required and is warranted by the statistical facts that 85 per cent of patients do survive an acute episode of myocardial infarction,[8] most patients recover from acute pulmonary edema and congestive failure, and the incidence, mortality and morbidity of acute rheumatic fever have improved considerably under the regimen of bed rest, antibiotics, ACTH, cortisone and salicylates. The importance of avoiding the transfer of the physician's anxiety to the patient cannot be overstressed.

Unknowingly severe emotional trauma is often produced by casual remarks by the nurses and house staff, and by learned discussion of prognosis in the patient's presence, especially when he is thought to be heavily sedated. During the period of acute illness, excessive restriction of the patient, prolonged narcosedation and prolonged unnecessary use of oxygen (especially if its use is not explained briefly to the patient as being therapeutic in the same fashion that digitalis and other medications are used) are some of the obvious but generally unappreciated methods of producing needless fears.

In summary, during the treatment of the acute episode it is important that the physician present a positive attitude which is hopeful and realistic, based on the knowledge that most patients recover from acute episodes of myocardial infarction, pulmonary edema and congestive failure.

After the acute crisis is over—There is a need to explain the immediate and long-term goals to the patient and his family. The patient will need help in accepting the fact of his heart disease. The patient should be informed in general terms of the plan of therapy, especially during the time of hospitalization and during convalescence. A concerted effort should be made to help the patient develop some insight into his disease and to encourage a receptive mood for future rehabilitation. From the very beginning a positive attitude must be maintained that the patient will eventually return to the competitive world successfully. Emphasis should be placed on the high recovery rate of patients with heart disease in general and of the excellent vocational readjustment which is now based on factual observations. In addition, the improvement in prognosis and therapy can be brought to the patient's attention indirectly.

If the patient has congestive failure, the regimen of dietary control, cardiac medication and action of diuretics should be presented to the patient in general physiologic terms. A simple description of heart function is well within the grasp of most patients. If the patient is hypertensive and obese, and weight reduction will be required, the general principles and importance of weight reduction should be presented.

If the patient has coronary artery disease, the concept of collateral circulation should be presented. Implanting and fostering the concept of collateral circulation has positive psychotherapeutic affects. In our opinion, the unfortunate analogy that arteriosclerosis is "like rust accumulating in pipes" is taboo, since the concomitant development of collateral circulation is ignored. Naturally, if the patient is told that he has had a coronary occlusion he may be overwhelmed by the anxiety that is associated with the term. He easily becomes depressed and fatalistically but reluctantly accepts the idea that his productive days are over. Unfortunately this can be confirmed in the patient's mind by admonitions from the physician that it is going to be necessary for him to change his "whole way of living." Nothing need be further from the truth. It will be stated later that 76 per cent of patients return to the same vocational and occupational classification.

Hospital Convalescence

Up to this moment the medical care has predominated in the management of the patient. During this period (which usually starts on the third to fifth day after admission, occasionally sooner, and ends approximately after three or four weeks in the hospital) the coverage and management of the patient differs. Here the team is organized and the team approach is put into action.

From the medical standpoint rehabilitation takes many forms. It is quite reassuring to the patient to be allowed use of a bedside commode and later, when he can walk safely, to be allowed use of the bathroom if it is no more than 10 or 15 feet away from the bed. Benton and associates have demonstrated that less energy is expended in using a bedside commode than in using a bedpan.[9] The value of the bedside chair in the treatment of myocardial infarction and congestive failure has been amply demonstrated by Levine.[10] Not only is it beneficial from the circulatory standpoint, but psychologically it removes the patient from the realm of complete bed restriction to that of relative liberty. Bedfast invalidism is prevented by such management. The patient is happier since the days seem considerably shorter in the hospital when he is able to sit comfortably several hours in a bedside chair.

In addition, medical management should be concerned with the prevention of the ill effects of excessive bed rest. During World War II, Keys and others demonstrated that excessively restrictive bed rest was associated with certain definite catabolic changes, loss of nitrogen, phosphorus, calcium, muscular wasting, decrease in skeletal muscle tone, bone atrophy, vasomotor instability, and decrease in cardiac output, blood volume, blood pressure, heart size and exercise tolerance.[11,12] Healthy normal young soldiers required from two to six weeks to recover their tolerance to moderate exercise. Many such healthy subjects restricted to bed for a period of several weeks manifested signs of neurocirculatory asthenia on resuming physical activity, i.e., a relatively rapid heart rate, a feeling of faintness and dizziness, weakness, asthenia and anxiety. Several days before ambulation, the patient should be instructed to exercise his legs by bending his knees and flexing and extending his ankles several times an hour. Patients with heart disease who have been excessively restricted may also suffer the ill effects of bed rest. It is important and reassuring to inform the patient of the normalcy of this response to early ambulation.

The patient should be encouraged to participate *actively* in his own rehabilitation. During his acute illness, necessarily he has "to renounce ownership" of his own body and permit it to be handled passively. He is dressed and undressed, fed, cleaned, washed, helped with urination and defecation, turned from one side to the other, his nakedness exposed to nurse and doctor, regardless of sex, of decencies and of conventional restrictions. He is, as it were, under orders subjected to a hygienic routine which implies a major disregard for his personal attitude and preferences. Characteristically enough, many adults sum up this experience as being "treated as a baby," or as "a complete return to conditions of their childhood."[13] This period of passivity should be abbreviated as much and as soon as possible. For the coronary and hypertensive patients enforced passivity is especially harmful, being the antithesis of their aggressive and dynamic personalities.

An educational program should be instituted at this time from other standpoints. If some form of dietary restriction is advisable the general philosophy of dietary control should be presented. The dietitian should have an opportunity to discuss special diets leisurely during several interviews with the patient and his wife. It should be made clear to the patient and his wife that a restricted diet does not mean a tasteless diet.[14] Great emphasis and care should be placed on preparing diets which are attractive as well as therapeutic. The physician should make available to the patient selected articles dealing with the adjustment of other patients to their heart disease. Such lay reading should be individualized. Care should be taken to avoid several publications now in print which empha-

size the restrictions rather than capabilities of persons with heart disease.

The work of the occupational therapist may be exceedingly important, particularly to the patient who is bored and unhappy during this period of enforced restriction. This is especially true of the patient with congestive failure who is necessarily restricted to bed. Occupational therapy may be therapeutic or diversional. By no means should it be limited to weaving of mats or leather grooving. In patients whose eventual occupational readjustment is highly dubious, a long-term program of diversional occupational therapy may be instituted.

During the convalescent period the full impact of the illness on the patient often becomes suddenly apparent. Consultation with and referral to a psychiatrist may be required in selected instances. However, superficial psychotherapy by the private physician usually suffices. The support and cooperation of the family to alleviate the patient's worry should be enlisted. It is desirable to exclude or minimize business worries whenever possible. The patient should not be allowed free access to the telephone and should not be allowed to conduct his business from his hospital bed. The physician may find it advisable in certain instances to make exceptions to these rules and to allow greater communication between the patient and his employers or associates. A few minutes of discussion of the patient with his employer or business associates may alleviate many anxieties. It is important to exclude visitors who disturb the patient. Usually the family and nursing staff can advise in such exclusion.

The social worker may play an important role at this time for patients in all economic strata. The social worker can help the patient to use community facilities and to delineate the nature of economic and family pressures. If the patient's wife is relatively young and if it is necessary for her to seek gainful employment, provision may be required to care for the children and to make other adjustments in the home.

During this period of early convalescence, as well as later, the advances the patient makes and is urged to make in the direction of rehabilitation must be consistent with the patient's physical and emotional progress. There is a need for individualizing the rate of physical and emotional rehabilitation. For example, some patients may benefit from thinking of returning to the world of work earlier than others. In some, the thoughts of returning to the competitive world may overwhelm the patient and produce severe anxiety. In such instances it is better to relegate such thoughts to the limbo of the future.

Treatment of Associated Complications

The rehabilitation of patients with heart disease may be modified by associated diseases (diabetes mellitus, renal involvement) and particularly by thromboembolic complications. Thromboembolic phenomena (to the brain, extremities, lungs, kidneys) are frequent in rheumatic heart disease and in myocardial infarction. Immediate recognition and early therapy reduces morbidity and mortality and enhances the possibility of maximum rehabilitation. In rheumatic patients hemiplegia may occur before or during mitral commissurotomy and, rarely, after operation. In view of the fact that heart surgery improves the cardiovascular function in such patients, vigorous treatment of the hemiplegia is indicated since they are relatively good candidates for retraining. The concurrence of thrombotic processes in the brain, kidneys and extremities in patients with arteriosclerotic heart disease usually is confirmation of the diffuse nature of the underlying arteriosclerotic process. However, recovery may be surprisingly good. We have seen several cardiac patients who have recovered from three or four episodes of cerebral artery thrombosis and have returned to employment.

The details of management and rehabilitation of the patient with hemiplegia have been summarized elsewhere.[1] The attending physician must recognize that the outlook for the hemiplegic patient is far from hopeless. The majority can be rehabilitated to be self-sufficient in the activities of daily living and many can be placed in selective jobs.

Shoulder-hand disability may complicate the late rehabilitation of patients with myocardial infarction. If restriction of shoulder and hand motion interferes with performance of a job, specific therapy is indicated.

Home Convalescence

The period of convalescence is variable and its duration is often difficult to define. During the home convalescent period the ultimate goal is to increase the patient's activities gradually and safely. At the present time the physician usually errs in the direction of excessive restriction and limitations. The time and rate of increasing the patient's activities must of course be individualized. In the patient with congestive failure not associated with myocardial infarction (e.g., rheumatic heart disease or hypertension), an equilibrium is generally established within a month. In patients with myocardial infarction, morphologic healing is well on the way six to eight weeks after the onset.

Diets—During the home convalescent period, dietary restrictions should be lightened whenever possible to a point that is bearable. The diet should be reasonable and practical to allow the patient to eat outside of the home later, if necessary, in the pursuit of his occupation. Severe restriction of salt is often advised routinely for patients with heart disease, even in the absence of congestive failure. This practice is not justified in our opinion. The mere presence of heart disease is not an indication for a low salt diet. However, a diet containing 2 to 5 gm. of sodium chloride is practical and can be palatable. In prescribing salt restriction for patients with hypertension but without congestive failure, the physician must recognize that salt intake must be less than 500 mg. to have hypotensive value.[15] Furthermore only one-fourth of patients with severe essential hypertension can respond favorably to prolonged restriction of sodium intake to less than 0.5 gm. daily.[15] Except for a few stalwarts, a diet containing less than 500 mg. is not feasible. The value of salt restriction must therefore be weighed carefully in the individual case.

The virtual impossibility of following a truly low cholesterol, low fat diet and the improved long-term value of such a stringent diet must also be recognized. The basis for a low cholesterol diet stems from experimental observations of cholesterol-fed chickens and hypothyroid dogs. Too little attention has been directed to the possibility that the low cholesterol diet may not influence directly the course of arteriosclerotic heart disease, except by weight reduction for the obese patient (which can be accomplished less unpleasantly). Furthermore, exogenous cholesterol is only one factor influencing the serum cholesterol level since isotopic studies have indicated that the body synthesizes cholesterol from readily available substrates such as acetates.[16] Thus dietary reduction in serum cholesterol is often temporary. It would seem reasonable, therefore, that only patients with a demonstrated disturbance of cholesterol and fat metabolism require such stringent diets.

In summary, unless there is a specific indication, mass prescription of restrictive unpalatable diets is not advisable. The inability to follow such diets often produces considerable anxiety in the average cooperative patient. Actually this anxiety may produce feelings and aggravate cardiac symptoms, thus interfering with the work adjustment period.

Removal of restrictions—An increase of activity allows more privileges and a methodical withdrawal of restraints. A positive attitude should be presented to the patient as to what is allowed rather than what is denied. A reasonable program would allow the patient gradually to eat more than one meal with his family, extend his bathroom privileges, allow him to go up and down a flight of stairs once a day for a few days and then several times thereafter, increase visitor's privileges, after two or more weeks short walks in the confines of his home and in his yard, short diversional automobile rides, and later allow him to drive the car himself. The patient should be permitted to increase his activities to the point of slight discomfort.

The desire to return to the world of work should be nurtured carefully and by design. This desire is nurtured by increasing the num-

ber of contacts with the outside world, removing restrictions and increasing liberties. The restrictions on tobacco and physical activities (including sexual) should be lifted individually. The categorical denial of tobacco to *all* patients must be condemned vigorously, especially in patients to whom occasional or moderate use of tobacco has significance. Most patients with heart disease can smoke moderately without apparent harm.[17] The studies of Levy indicate that the effects on the heart of moderate smoking are relatively slight and are no greater in patients with heart disease than in normal persons.[18] The private physician can detect sensitive patients clinically if angina, increase of blood pressure, or increase of pulse rate (more than 20 per minute) occurs after the patient smokes one or two cigarettes. Nicotine sensitivity can also be demonstrated by recording electrocardiograms and/or ballistocardiograms before, during and after the smoking of one or two cigarettes.[19]

In summary, if tachycardia, or angina develops in such tests, if the ballistocardiogram becomes abnormal, if there are significant electrocardiographic changes, and if there is significant peripheral vascular disease, restriction of tobacco is probably warranted.

Evaluation of the fitness of the patient during the home convalescent period—The fitness of the patient is reflected in his reaction to increased activity. It is important to recall the easy fatigability of the normal person who has been restricted to bed. Increased angina, fatigue, appearance of congestive failure, arrhythmias, tachycardia, palpitation and certain electrocardiographic changes are clinical indications of deterioration. The evolutionary T wave changes found in the development of a myocardial infarct should not be misinterpreted as indicating deterioration.

Clinical measures of cardiac reserve—The available clinical measures of cardiac reserve unfortunately are not employed routinely by the practicing physician. The electrocardiogram exercise tolerance test is used widely and often interpreted solely as a measure of the coronary circulation. For a more complete evaluation other parameters of the cardiopulmonary system should be measured. These parameters of cardiopulmonary function have been clearly defined in the clinical physiologic laboratory and can be used readily in the home and office. Bruce and others[20,21] have defined physical fitness using the following parameters: blood pressure, respiratory rate, maximum heart rate during exercise, and duration of the period required for recovery. In the performance of work which consists of two to five times the resting oxygen energy cost, a fit person with or without heart disease develops a respiratory rate no greater than 25 per minute during exercise, a heart rate of less than 125, and, within the first three minutes after the cessation of exercise, the heart rate, blood pressure and respiratory rate will return to resting levels.[20,21] The reciprocal of the respiratory rate has been shown to be a good measure of respiratory efficiency (that amount of oxygen removed from each 100 cc. of air breathed).[20] The electrocardiogram will show diminution of the T wave, no ectopic beats, and ST displacement of less than 1.0 mm.

The value of the ballistocardiogram in the evaluation of cardiac function during rehabilitation is still under considerable dispute. There seems to be some correlation between the normalcy of the ballistocardiogram at rest and the ability to do measured work.[21,22] However, for patients over 50 years of age, the ballistocardiogram cannot be used to evaluate physical fitness.[23] In our studies[21] we have found that if the ballistocardiogram is normal, the patient with heart disease has a better chance of having a normal fitness index and capacity to perform work on a treadmill. On the other hand, if the ballistocardiogram is abnormal, a significant number (44.0 per cent) may still have normal fitness.

Evaluation in the home environment—The best method of determining the patient's functional capacity is to observe him during the time of performing specific work at home or on the job. The physician is in a good position to observe the patient in his home and to make a clinical physiologic evaluation. The response to an energy load of climbing up and down a flight of stairs (approximately 15 steps) in one minute can be readily deter-

mined. The physician should take the respiratory rate, blood pressure and heart rate before this exercise, observe the patient during the period of the exercise and immediately thereafter and note the rate of recovery in the following five minutes. As an adjunct, electrocardiograms may be taken. If recovery takes longer than three minutes, this amount of exercise must be considered excessive. If there is no clinical or physiologic evidence of embarrassment with the energy expenditure of climbing one flight of stairs, and if return to normal of respiratory and heart rates is complete within three minutes, it is safe to assume that the exercise may be increased. At a later date, after gradual training, the duration of the test may be increased to a maximum of 10 minutes.

In our experience one-half of the patients with myocardial infarcts improve physically within three months to be able to expend two to five times the resting oxygen consumption without difficulty. This energy cost is approximately equivalent to climbing steps at the rate of 15 per minute for 5 to 10 minutes.

Another simple test of fitness has been described by Karpovich and associates.[24] Patients make 12 complete step-ups (with both feet) on a bench 12 inches high in 30 seconds. If the pulse rate, taken 60 to 90 seconds after exercise, is 100 per minute or less, the patient is considered fit for physical activity. After several or more days, a second test is performed, consisting of stepping up and down (with both feet) on a bench 20 inches high at a rate of 24 steps per minute, as long as he can, but not in excess of five minutes. Perhaps a bench 16 or 18 inches high would be preferable. The response to serial tests serves as an objective guide to the physician in regulating the rate of physical rehabilitation of the individual patient.

The physician should also observe the patient's reaction to other ordinary activities in the home and determine the patient's therapeutic and functional classification employing the New York Heart Association criteria.[25] This classification depends entirely on clinical judgment and does not attempt to assess the patient's ability physiologically to do a known amount of work. From this classification and the physiologic evaluation, the physician is better equipped to advise on the next step in rehabilitation.

When the patient has advanced to the point that he is able to withstand an estimated expenditure of energy of two to three times resting level, has made an emotional recovery, and has had a return of temperature, pulse, respiration and sedimentation rate to a fair control level, consideration should then be made for the return of the patient to the occupational world.

Work Adjustment Period

The work adjustment period may begin anywhere from two to four months after the acute episode. The purpose now is to return the patient to a competitive productive life commensurate with his abilities and recognizing his limitations. It has been assumed that the work motivation has been stimulated in earlier phases. However, because of individual variation in the rate of recovery in selected instances the work motivation may be very poor, underdeveloped or stifled.

At this time there is a real need for action by the team to make the best of the patient's physical and mental capacity to lead to selective placement. At this time the team ideally consists of the private physician, industrial physician, employer (personnel manager or foreman), vocational counselor and social worker.

The basic problem is to determine and match the patient's total capacity with the demands of a specific job. The difficulty many physicians have in finding time to delineate the nature of the patient's job does not obviate the necessity of obtaining the facts. An attempt can be made to evaluate the patient other than from a medical standpoint alone. The physician who disposes of his cardiac patients by a general placebo prescription addressed to the employer or his industrial physician stating, "Give this man a light job," does not solve the problem of selective placement.

Matching the patient's capacity with the demands of a specific job can usually be done

most efficiently by the team approach as in work classification units.[26] In the absence of such a unit the principles of the team approach can nevertheless be employed successfully by the private physician in most communities.

The patient's "total physical capacity" can be evaluated satisfactorily by the private physician. As mentioned before, the patient's response to the work load of walking, bending, lifting, stair climbing, can be observed and measured. The energy cost of such exercise later can be equated roughly with the job demands. The work of walking at 1.7 miles per hour on a 10 per cent grade for 10 minutes or climbing standard nine inch steps at the rate of 20 per minute for 10 minutes entails an expenditure of three to four times the resting level. Although there is a great deficiency of knowledge of energy requirements on a job, it has been well demonstrated that moderate heavy work requires three times basal oxygen consumption and strenuous work approximately eight times basal oxygen consumption.[27] It is our impression that over half of the jobs in American industry require no more than two to four times resting energy metabolism. It has been shown, for example, that sawing wood requires 2 to 2.5 times resting oxygen consumption, filing and sanding 1 to 1.5 times, and wood assembling no more than 2 times resting oxygen consumption.[1] The energy demands of many jobs are relatively low and except at peak loads, do not exceed two to five times resting oxygen consumption. This is well within the capacity of most cardiacs with a classification of better than III. Compensated cardiacs and noncardiacs require the same amount of energy to perform similar work of the above magnitude. This of course assumes equal skills.

The private physician then may attempt to evaluate the demands of the job from a job description in order to make more specific recommendations. A conference of the industrial physician, private physician and employer (or his representative) should ordinarily be sufficient to effect selective placement of most patients with heart disease in the place of their last employment. This is true since 76 per cent of cardiacs can remain in the same occupational and industrial classification, a tribute to the technical development of American industry.

If selective placement cannot be effected in this fashion the private physician may enlist the help of other disciplines . . . vocational counseling and testing, rehabilitation service and placement services.

The conscientious physician thus finds himself burdened with cares seemingly far removed from the "pure" domain of medicine. In approximately 14 cities there are special work classification clinics which relieve the private physician of such responsibilities. Because of the success of The Cleveland Work Classification Clinic, we believe it worth while to describe its operation in some detail so that the reader may consider the establishment of a similar unit in his own community.

Several years ago a survey in the Cleveland area indicated that patients with heart disease had great difficulty in being rehired, in obtaining new jobs and that they were often saddled with unnecessary restrictions. There was a reluctance of management and industrial physicians to take new risks in the form of hiring old or new employees with heart disease. In addition there were many seniority rules which precluded the assignment of persons with heart disease to jobs which are lighter and often more highly sought after under seniority rules.

Five hundred patients with heart disease have been studied in the past three years. These patients have represented a nonindigent, highly productive working population of stable work background, representing the real world of work in Cleveland. These patients were home owners and substantial citizens. They were skilled and represented all the major job classifications.

The clinic team of the Work Classification Clinic consists of a cardiologist, vocational counselor and medical social worker. The social worker is interested in the pre-illness personality, temperament, attitude of the patient, the meaning of the illness to the patient, his intellectual and emotional understanding of his disease, his family problems and economic

problems. The vocational counselor of the team obtains detailed information as to the job history, skills, education, work attitude, personality needs, work motivation, job features, demands, transportation problems and the exact details of the present or last employment. The cardiologist is interested in determining not only cardiac structure but also function. Emphasis is placed on the function of surviving tissue, recognizing the importance of the extent of the structure impaired by disease. In addition to a complete history and physical examination, fluoroscopy, blood analysis and exercise tolerance tests are performed. The latter includes walking over two standard nine inch steps and in a select number walking on a treadmill to determine the function of the heart and lungs.[21]

After a complete evaluation of the patient on one clinic day, the social worker, vocational counselor and cardiologist confer and discuss the patient, having observed him in the same phase of his illness. A detailed practical work recommendation is made and forwarded to the private and industrial physician. When necessary the vocational counselor visits jobs to determine their requirements. Personal communication with management, employer, personnel, union representatives, etc., expedite and facilitate the implementation of the recommendations of the clinic team.

The needs of patients with heart disease at the time of the clinic visit are multiple, indicating the diversity of their problems. Thirty per cent of the series studied required vocational guidance, 20 per cent vocational rehabilitation, 10 per cent physical rehabilitation to improve work tolerance, 8 per cent needed avocational guidance and 80 per cent needed emotional and intellectual interpretation and supportive reassurance. From the complexities of the needs of these patients, it would seem that the nonintegrated approach and the final management of the majority of such cases by one physician alone would have been inadequate. As mentioned before, the emotional problems were second in importance to heart disease. In 46 per cent of the cases the emotional impact of the illness on the patient was far more important than the organic heart lesion itself. Forty-two per cent of the patients with heart disease were unable to face their illness, this being worse in the younger coronary or younger rheumatic patients, possibly because they have not yet had the time to develop a philosophic acceptance of disease that older people have.

The origin and nature of the emotional problems have been mentioned earlier. Patients with hypertensive or coronary artery disease particularly over-reacted emotionally, being overwhelmed by the fact of the disease, over-restriction and the physician "induced contraction" of their world.

The disposition of the patients after the initial visit differed slightly from their needs mainly because all patients could not accept the recommendations. Thirty per cent of the patients were referred to placement services for selective placement and in 21.8 per cent recommendation was made for job transfer within the plant. Thirteen per cent utilized vocational counseling services (this group included patients who need long term vocational planning especially those with congenital heart disease, mitral surgery and young coronaries). Twelve per cent were referred to the sheltered workshop of the Cleveland Rehabilitation Center to improve work tolerance and motivation; 11 per cent were advised to return to their physician for more medical therapy, due to changes in the cardiac status between the last visit to the physician and the clinic; in 8 per cent of the cases formal psychotherapy was suggested. Family agencies were used in 4 per cent of the cases.

In follow-up studies the practical value of selective placement by industry was demonstrated. Over a period of three years the cardiac status improved twice as frequently as it deteriorated. The majority of patients (65 per cent) remain in status quo. From the occupational standpoint, there was a greater improvement, since three times as many improved as got worse. The improvement in the cardiac and occupational status indicates a fallacy in the current concept that the course of heart disease is progressively downward. Follow-up studies revealed that of the original

group who were unemployed at the time of the first visit, 60 per cent were employed by competitive industry on a subsequent visit. Frequently it was possible to modify the job or the worker's responsibility to the job. The extension of privileges, changing the location of the locker, or allowing parking nearer to the plant removed distressing features of a job. The financial earnings of these previously unemployed patients has been estimated to total $600,000. Considering that the cost is less than 2 per cent, this is a material accomplishment. The clinic team approach of the Work Classification Clinic enabled patients with heart disease to return to the status of a wage earner, to gain selective placement, to obtain new jobs, to work safely in a variety of occupations and industry, and to adjust more satisfactorily to their heart disease.

Summary

The factors important in the rehabilitation of patients with heart disease include (1) nature and course of heart disease, (2) emotional reaction, (3) iatrogenic disability, (4) vocational features and (5) other diseases of significance.

In view of the complexities of rehabilitation there is a need for a team approach in order to integrate multiple disciplines: medical, psychiatric, social, vocational and occupational. The composition of the team and the relative importance of its members vary during the three phases of rehabilitation: acute illness, convalescence and return to the world of work. A plan is presented in detail to prevent iatrogenic disability and cardiac neurosis, to expedite physical and emotional rehabilitation and to minimize the effects of excessive bed rest. The physician is urged to evaluate the patient's functional capacities in physiologic terms in order to regulate the rate of rehabilitation.

Matching the patient's capacity with the demands of specific jobs (selective placement) can usually be done most efficiently by work classification units or through the cooperation of private and industrial physicians and of management.

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Pediatrics IN GENERAL PRACTICE

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Vitamin K in the Treatment of Hemorrhagic Disease of the Newborn

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IN 1935, vitamin K was found to be a factor necessary for the prevention of a hemorrhagic disease in chicks. The prophylactic and curative effects were shown to be due to the fact that normal blood coagulation, more exactly normal prothrombin activity, could be maintained only when vitamin K was supplied in the diet.† Lack of vitamin K as a factor in human disease was first demonstrated in 1938 in connection with the so-called cholemic bleeding tendency in obstructive jaundice. Here the vitamin K deficiency is due to deficient absorption of natural fat-soluble vitamin K in the absence of bile.

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The relationship between vitamin K and hypoprothrombinemia and hemorrhagic disease in newborn infants was recognized in 1939 and has been the subject of numerous investigations since then. Most investigators, including ourselves, have found that while the

†The naturally occurring forms of vitamin K are vitamin K_1 (2-methyl-3-phytyl-1,4-naphthoquinone) from green leaves and vitamin K_2 (2-methyl-3-difarnesyl-1,4-naphthoquinone) from many bacteria including *Esch. coli* and *B. bifidum*. Both these forms are yellow, fat-soluble and insoluble in water, but an aqueous colloidal solution of vitamin K_1 can be prepared, and it is used to neutralize the effects of anticoagulants of the DICUMAROL® type, as well as for other purposes.

The parent substance of the natural vitamins K, 2-methyl-1,4-naphthoquinone (menadione, U.S.P.) is also highly active against vitamin K deficiency. Menadione is a yellow crystalline powder, slightly soluble in water at body temperature. Menadione bisulfite (U.S.P.), prepared by boiling menadione in water with sodium bisulfite, is water-soluble and available for parenteral use. Also available for parenteral use are the colorless salts of 2-methyl-1,4-naphthohydroquinone diphosphoric acid (SYNKAYVITE®). Synkayvite prepared for parenteral administration is usually the tetrasodium salt; Synkayvite in tablet form for oral administration is usually the dicalcium salt.

On a molecular basis, the simpler compounds are about equally potent as are vitamins K_1 and K_3, in relieving vitamin K deficiency, but unlike vitamins K_1 and K_2 they are not active against anticoagulants of the Dicumarol type.

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TABLE 1

INCIDENCE OF HEMORRHAGE AND PROTHROMBIN CONTENT OF THE BLOOD*

NUMBER OF INFANTS	PROTHROMBIN TIME *(seconds)*	PROTHROMBIN *(per cent)*	INFANTS WITH HEMORRHAGE	
			Number	*Per cent*
969	100	7.0	53	5
178	300	3.5	23	13
25	1,000	2.5	9	36

*Prothrombin time was estimated at the time of bleeding in infants with hemorrhage and at the age of two to four days in infants without hemorrhage.

prothrombin activity of the mothers is considerably increased at the end of pregnancy, prothrombin activity of the newborn is lower than that of infants a few weeks old, which again is lower than that of children one year old and of adults. The prothrombin activity at birth is usually between 20 and 50 per cent of the normal value for adults. It is of particular interest that, according to Larsen,[1] much lower values—down to a few per cent—are found in infants who have suffered intra-uterine asphyxia to the extent that the amniotic fluid is colored by meconium. The increased capillary fragility engendered by anoxia concomitant with extremely low blood coagulability combine to make hemorrhage a great risk, especially in premature infants.

Administration of vitamin K to the mothers immediately before or during labor does not cause any important increase of prothrombin activity in nonasphyctic infants at birth. Thus, the physiologic hypoprothrombinemia at birth is largely unrelated to vitamin K. Limited experimental evidence, however, suggests that maternal treatment with vitamin K has a greater influence on the prothrombin activity of asphyctic children at birth. This point requires further investigation.

The variation of prothrombin activity during the first week of extra-uterine life follows a characteristic course. During the first two to four days prothrombin activity declines slightly, but toward the end of the first week it increases relatively fast. From then on the increase is slower until a constant level, identical with that of normal adults, is reached at the age of about one year. This course is characteristic for normal breast-fed infants, whereas, in artificially fed children the decline of prothrombin activity in the first week is usually not found.

Administration of vitamin K to mothers immediately before or during labor, or to infants at birth, will nearly always eliminate the decline of prothrombin activity seen in breast-fed infants. Thus, the decline in prothrombin activity usually occurring in normal breast-fed infants in the first week must be due to a normally occurring, low supply of vitamin K.

The most likely explanation of the decline and following rise of the prothrombin activity of breast-fed infants in the first week is that not until the third to fourth day, when the milk "comes in," is the supply of vitamin K through the milk sufficient to insure a synthesis of prothrombin high enough to exceed or equal its metabolic destruction. The vitamin K content of breast milk is low, but it is apparently sufficient to meet an infant's requirement which has been found experimentally to be only about 10 γ a day. As a routine measure, however, it is more practical to give a single dose of 10 mg. of Synkayvite intramuscularly to the infant at birth, or 40 mg. of Synkayvite or an aqueous colloidal solution of vitamin K orally to the mother just before or during labor.

Hemorrhagic disease of the newborn is seen in 0.1 to 1 per cent of all newborns when no vitamin K is given. The hemorrhages most frequently appear about two to four days after birth. In rare cases they are seen at birth, and still more infrequently after the first week. The hemorrhagic tendency manifests itself as hematemesis, melena, umbilical and skin bleedings. The degree of severity may vary from quite mild to fatal. Before the advent of vitamin K therapy, the only effective treat-

TABLE 2

INCIDENCE OF HEMORRHAGIC MANIFESTATIONS IN NEWBORN INFANTS*

TYPE OF HEMORRHAGE	NUMBER OF CASES PER 10,000	
	Vitamin K to mothers†	*No vitamin K to mothers*
Melena	6	16
Umbilical	1	9
Adrenal	5	15
Subcapsular hepatic	12	18
Intraperitoneal	2	8
Cutaneous	20	23
Cephalhematoma	105	111
Intracranial	123	163

*The series comprises 10,876 infants whose mothers received vitamin K, and 22,371 infants whose mothers were not given vitamin K.

†Given 1 to 24 hours before delivery.

ment available was blood transfusion.

The question arises whether there is any causal relationship between low prothrombin activity due to insufficient supply of vitamin K and the appearance of hemorrhage. As is well known from hemorrhagic diseases in general, bleeding is always initiated by a vascular, even a capillary lesion. It may therefore not follow, *a priori*, that every infant with low prothrombin activity will show signs of hemorrhage. On the other hand, one must expect that there will be more infants with hemorrhages among those children whose prothrombin activity is very low than among those who have a higher prothrombin activity. That this actually is the case appears from table 1.[2]

It would be expected that the prophylactic administration of vitamin K to the mothers would lower the incidence of hemorrhages in the newborn. This was investigated by Dyggve[3] and a summary of his results is presented in table 2.[3]

It can be seen that the characteristic manifestations of hemorrhagic disease, viz., melena and umbilical bleeding appear considerably less frequently in the group treated with vitamin K. Thus, it is evident that administration of vitamin K to the mothers is of definite prophylactic value. It should be emphasized that comparison between groups of treated and nontreated mothers can be made only when the groups are large enough and otherwise comparable.

It is striking that internal bleeding, viz., adrenal, subcapsular hepatic, intraperitoneal and intracranial, also occurs less frequently in the treated group. Since these internal hemorrhages are clinically and numerically more important, it is a noteworthy difference. A closer analysis of the group of intracranial hemorrhages revealed that the difference in frequency was considerably greater in premature than in full-term infants. This might indicate that vitamin K prophylaxis will decrease the frequency of intracranial hemorrhages in prematures. As previously mentioned, anoxia predisposes both to low prothrombin activity and to increased capillary fragility, which might explain the fact that intracranial hemorrhages are frequent in asphyxiated prematures.

Opinion is divided as to whether vitamin K should be given prophylactically in all cases. Since it is very difficult or impossible to decide beforehand in which cases prophylactic administration of vitamin K is indicated, and since prophylaxis is inexpensive and safe, we feel that vitamin K should be given as a routine measure to all mothers just before or during labor.

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Toxoplasmosis

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IN the last decade the etiology, pathology and clinical manifestations of toxoplasmosis have been sufficiently clarified to classify it as a distinct disease entity. The protozoon, *Toxoplasma,* may be the causative agent of chorioretinitis, rash, jaundice, hepatosplenomegaly, meningo-encephalitis, hydro- or microcephalia, convulsions, mental retardation, intracerebral calcifications and pneumonitis in the neonatal period or early infancy. Certain cases of encephalitis in adults and children, as well as a spotted fever syndrome, also have been traced to *Toxoplasma.*

Historical

A *Toxoplasma* infection was first described in the Java sparrow by Laveran in 1900, and later in the African rodent, the Gondi, and in the rabbit. Nicolle and Manceaux, in 1909, proposed the name "*Toxoplasma gondii*" for the parasite. Since then there have been many reports of the natural occurrence of the organism in a variety of species of mammals and birds. This history of *Toxoplasma* and toxoplasmosis was well reviewed by Sabin.[1]

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The first human cases of toxoplasmosis were described by Castellani in 1913 and by Janku in 1923. In 1937, Wolf and Cowen[2] reported several cases in infants with complete clinical and pathologic studies and established toxoplasmosis as a disease entity. In 1940 the first proved adult case was reported by Pinkerton and Weinman.[3]

The Parasite

The *Toxoplasma* organism exists in extra- and intracellular forms. The extracellular organisms are crescent-shaped and measure from 4 to 7 micra in length and 2 to 4 micra in width. With Giemsa-stained preparations,

well-defined nuclear chromatin and a distinct and clear cytoplasm are visible. All current evidence indicates that the *Toxoplasma* is a protozoon, and that there is only one serologically distinguishable type.

The intracellular form is usually oval or round and the cytoplasm is less distinct, particularly when the parasites are closely packed within the host cell.

The *Toxoplasma* readily invades practically all types of fixed tissue cells, particularly reticuloendothelial cells. It multiplies exclusively by longitudinal binary fission and only within living cells. When observed in microtissue cultures, the cycle of the organism within the host consists of: (1) invasion of a tissue cell, (2) rapid intracellular multiplication of the parasite, (3) distention of the cell, and finally, (4) rupture of the cell membrane with release of parasites into the surrounding tissue fluids. The cycle is repeated with active invasion of other cells.

Development of immunity by the host modifies the cycle of the parasite. Fewer organisms are present and multiplication is slowed down. Infected host cells no longer rupture as readily and the cytoplasmic membrane persists as an envelope around tightly-packed masses of *Toxoplasma*. These cells entirely filled with *Toxoplasma* are called "pseudocysts" and their presence is a sure sign of some degree of host immunity.

Pathology

The pathologic features of *Toxoplasma* lesions are similar, regardless of the tissues affected. Cerebral and spinal cord lesions are multiple, disseminated, and range in size from minute nodules to nodules several centimeters in diameter. They are yellowish in color, soft or cystic centrally, glassy at the margins, and they may contain gritty, calcific material. Heart lesions appear as yellowish irregular spots; lesions of the spleen and liver are usually grayish and wedge-shaped. In addition the lungs show proliferation of connective tissue and considerable thickening of the alveolar walls.

Stained microscopic sections consist of rounded necrotic foci with fibrinoid material replacing normal tissue elements, and miliary granulomas composed of neutrophils, eosinophils, plasma cells, epithelioid cells and macrophages. The transition between involved areas and normal tissue is usually sharply defined. Few or no *Toxoplasma* are visible and they do not parallel the degree of tissue destruction in active cases.

In chronic cases, parasites may be found as large intracellular masses of organisms, the so-called pseudocysts, without accompanying tissue destruction. The host is unable to eliminate the pseudocysts which persist for months or perhaps even for years. They do not seem to harm the host. Despite the persistence of these pseudocysts containing fully viable organisms, there is a rapid drop in the protective antibodies in experimental animals and this fall does not precipitate a flare-up of the infection.

Epidemiology

The route of human transmission of the parasite has not been established except in congenitally acquired infections. That the infant becomes infected in utero is certain. Advanced disease has been reported in newborn infants delivered by cesarean section with no clinical disease in the mothers. Death of the infants occurred within a few hours after delivery. Maternal serologic studies, however, invariably demonstrate high titers of neutralizing antibodies, thus proving the presence of subclinical infections in these mothers. Weinman[4] produced chronic, asymptomatic toxoplasmosis in mice and Eichenwald[5] subsequently showed that these animals could infect their offspring in utero but only in the early stage of the infection. This appears to be the reason why succeeding siblings do not become infected. There is no adequate evidence that a mother who has given birth to one infant with toxoplasmosis will infect subsequent children.

In the United States, subclinical toxoplasmosis is quite common; surveys have shown that the figure is negligible in early childhood, but it may reach 30 per cent and higher in the 30 to 40 year group.[6] The epidemiologic significance of this large carrier population is

not known. Furthermore, there exists a large reservoir of chronic and active infection among mammals and birds, both wild and domesticated. The importance of pets as possible sources of human infection has recently been emphasized.[7] Insect vectors have also been postulated. Lactating, infected animals can transmit the parasite in their milk.[5] This suggests the possibility of postnatal infection in humans and the spread from infected milk of cows and goats to man.

Clinical Manifestations

As shown in table 1, human toxoplasmosis may be classified as (1) acute, (2) subacute and (3) chronic, and each in turn may be symptomatic and asymptomatic. Clinical illness may be apparent in any, all or none of the stages of the infection.

Early toxoplasmosis is a generalized infection involving many organs. Repair of the extraneural lesions results from a developing immunity which evokes fibrosis of the lesions and mononuclear and eosinophilic infiltration characteristic of repair. The immune response is not nearly as active in the neuroectoderm. *Toxoplasma* continue to proliferate in nervous tissue after their disappearance from other viscera. This fact explains the predominantly neurologic signs and symptoms found in subacute and chronic toxoplasmosis.

In our series of more than 130 cases, about 35 per cent of the infants were admitted with histories compatible with a generalized infection: vomiting, drowsiness, twitching or frank convulsions, fever, leukocytosis, jaundice and hepatosplenomegaly. Spinal fluids in these acute cases were always abnormal, whereas in the more chronic cases with predominantly neurologic signs, they were frequently within normal limits. A detailed analysis of this series of patients is now being prepared.

Chorioretinitis was present in 80 per cent of our cases and it was the most important single clinical finding. Retinal examination reveals bilateral focal, more rarely multiple lesions, with macular involvement. The changes include local edema, necrosis, foci of atrophy and pigment deposits at the periphery of the lesions. Other ocular changes are rare. The

TABLE 1

CLASSIFICATION OF HUMAN TOXOPLASMOSIS
(Modified after Frenkel[8])

ACUTE TOXOPLASMOSIS—Generalized infection involving all age groups and all organs	
	Symptomatic Meningo-encephalitis, hepatitis, pneumonitis, myocarditis, rash, jaundice, etc.
	Asymptomatic Mothers giving birth to infected infants
SUBACUTE TOXOPLASMOSIS—Persistence of organism in the central nervous system, including the eye; all ages	
	Symptomatic Early calcifications, chorioretinitis
	Asymptomatic Detected serologically
CHRONIC TOXOPLASMOSIS—Central nervous system, perhaps eye and muscle; all ages	
	Symptomatic Microcephalia, hydrocephalia, convulsions, ocular malformations
	Asymptomatic Calcifications, serologic evidence

combination of intracranial calcification, chorioretinitis, psychomotor disturbances, and hydro- or microcephalia, was practically diagnostic of toxoplasmosis, as confirmed by significant serologic titers.

Onset of the clinical disease in most infants is shortly after birth; it rarely occurs as late as the first year or in childhood. Occasionally, fetal abnormalities are noted in utero—most often hydrocephalia. Convulsions or muscular spasm occur in a majority of patients but meningeal signs seldom appear and spinal and bulbar involvement such as paralysis of the extremities, difficulty in swallowing, and respiratory distress are late and rare occurrences. Internal obstructive hydrocephalia is noted early in about one-fourth of the cases and it is often rapidly progressing.

Associated extraneural visceral symptoms indicate that the immune responses of the host have not developed to the point of inhibiting the free multiplication of *Toxoplasma*. Hepatomegaly, splenomegaly, irregular fevers, jaundice, purpuric spots, anemia, maculopapular rash, electrocardiographic changes consistent with myocarditis, pneumonitis, or

pneumonia with pleural effusion, or severe diarrhea, all have occurred in one or more of our cases. It is this confusing array that makes the clinical diagnosis of acute toxoplasmosis so difficult in the absence of serologic studies.

In skull x-rays, the major diagnostic feature is the occurrence of widespread intracerebral calcifications, usually appearing either as small foci 2 to 3 mm. in diameter or in thin linear streaks 1 cm. or more long. These lesions, usually present at birth, are prone to occur in the region of the thalamus or the basal ganglia and are often symmetrical.

The cerebrospinal fluid may be xanthochromic under increased pressure, of high protein content up to a gram per 100 cc., and with a mononuclear pleocytosis seldom exceeding 200 cells per cubic millimeter. Sugar content is usually normal. *Toxoplasma* can only rarely be demonstrated in the centrifuged sediment of spinal fluid, either by direct examination of Giemsa-stained smears or preferably by intracerebral inoculation into mice or guinea pigs.

Serology

Serologic studies are the most useful tool for establishing the diagnosis. They are: (1) the neutralizing antibody reaction, (2) the complement fixation test, (3) the dye or cytoplasm-modifying test, and (4) the dermal sensitivity test. Each has its advantages and disadvantages.

The neutralization reaction consists essentially of incubating various dilutions of ground-up infected mouse tissue with test and control serums and injecting the mixtures intracutaneously into the back of a rabbit.[9] The degree of protection, as demonstrated by the extent of skin necrosis, is an index of neutralizing antibody titer. The disadvantages of this method are: The titer is invariably low; the method is time-consuming; it requires the use of an expensive animal, and the results are frequently equivocal. This test is no longer employed as a diagnostic tool.

The complement fixation reaction has the advantages of giving prompt results, of not requiring living *Toxoplasma*, and of being quite specific. Titers in active infection range from 1:2 to 1:64, and higher numerically.[10]

The best test is the vital staining reaction or the so-called dye test of Sabin and Feldman.[11] This method is simple, rapid and sensitive and is based on the phenomenon that the presence of specific antibodies alters the vital staining properties of the *Toxoplasma*. In infants with the disease, titers practically always exceed 1:256, and may go as high as 1:20,000. Its one disadvantage is that it requires living *Toxoplasma*.

The dermal sensitivity test is still a subject of controversy.[12] Although it is of value in public health surveys, our experience indicates that it should be used clinically only in conjunction with other serologic methods. With the available antigen, false positives occasionally occur and false negatives are frequent, particularly in infants. The test is, of course, the simplest of all and it is performed and recorded just like the Mantoux reaction.

A *Toxoplasma* diagnostic laboratory has recently been established by the U. S. Public Health Service and serums may be forwarded to this laboratory through any state health department.[12]

Proper evaluation of serologic tests entails the following considerations. A certain percentage of the normal population has been shown to carry antibodies to *Toxoplasma*. Passive transplacental transmission of antibodies from mother to infant also has been demonstrated.[13] A mother with a high level of antibodies can transfer these to the fetus without actively infecting the infant with *Toxoplasma* in the postnatal period. The high serum titer in the infant can persist for as long as six weeks before falling. A diagnosis of congenitally acquired toxoplasmosis, therefore, requires the demonstration of the persistence or elevation of the antibody titer in the infant over a period of several months. In addition, Sabin[10] has shown that in acute, highly active toxoplasmic infections in infants, neutralizing antibodies may be present in the absence of complement-fixing antibodies, even though the mother possesses both. In experimental animals, and in one human case, Eichenwald has also shown that the dye test titer, being most readily detect-

able, rises first, to be followed in about two weeks by a rise in the complement-fixing titer. In our patients, the complement-fixing antibodies disappeared first, usually within two years after the acute infection, whereas neutralizing antibodies and dermal sensitivity have persisted in all of our 10 patients with congenital toxoplasmosis who have been followed for five years or longer.

A definitive diagnosis of toxoplasmosis should not be made unless (1) there is adequate serologic evidence of the disease, or (2) the parasite is isolated from material obtained from the patient, or (3) typical tissue changes are found at autopsy and the presence of the organism demonstrated.

Treatment

Treatment of the disease is discouraging. Since most infants with toxoplasmosis are born with irreparable central nervous system damage, even if a drug which could eradicate the infection were available, a damaged child would still result. What is more, currently available drugs are not efficacious. It has long been known that the sulfonamide drugs have some inhibitory and, under certain conditions, curative action in the experimental disease; in the human form of the disease, results have been disappointing. Eichenwald[14] has reported that the combination of potent antiserums and sulfadiazine gave the best survival in mice but our clinical experience with this combination has been sparse and only moderately encouraging. Perhaps the most promising recent development in the chemotherapy of toxoplasmosis is the demonstration that the new pyrimidine drug Daraprim has a definite therapeutic effect in experimental infections and acts synergistically with the sulfonamides.[15] The over-all mortality rate in our recent experience averages about 15 per cent.

Follow-up studies on surviving patients are most discouraging. About one-half continue to have convulsive episodes; about 75 per cent show mental retardation, usually of severe degree; about 60 per cent show considerable loss of visual function.

Our chief hope in reducing the toll of toxoplasmosis lies in continued study of the epidemiology of the disease. Eichenwald has been able to prevent infection of the fetus under laboratory conditions; perhaps detection of the infection in pregnant women will permit similar prophylaxis. Only when the portal of entry of the *Toxoplasma* in humans is discovered, will the whole problem be intelligently and effectively attacked.

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Editorials

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THERAPEUTIC DENTIFRICES: CLAIMS AND FACTS

PHYSICIANS and dentists are observers in an advertising trend which involves them. Television permits the advertising of nostrums to the public with actors playing the part of the "doctor," advising patients about dentifrices, laxatives and vitamins, or reporting the results of "research" in the ad-writer's conception of a research laboratory. The volume of sales and the classification of dentifrices as cosmetics has made them the special target of the "pitchman."

It is claimed, or cleverly implied, that dentifrices will all but eliminate the problems of tooth decay, gingivitis and bad breath. Investigations have shown that brushing the mouth with *any* dentifrice will reduce odors originating about the teeth for varying times but will neither prohibit the decomposition of proteins left behind nor stop extra-orally originating odors.

Chlorophyll-containing dentifrices are given special odor eliminating powers by the advertisers but, scientifically, they have not been demonstrated as having any special power of removing or preventing persisting mouth odors. Of course, in the ad-writer's world chlorophyll-containing dentifrices are also supposed to prevent tooth decay, although no data adequate to support this claim have been published in scientific or professional journals. Newspapers and television showed a group of youngsters from a famous youth center smiling happily after they were "cured" of gingivitis by chlorophyll-containing toothpaste. Study of the published data shows no cause for the overly optimistic advertising for, while there was some difference at the end of a three months' study, at the nine month report the boys using nonchlorophyll dentifrice had benefited to the same degree as those using the green dentifrice.

Ammoniated, or more accurately "ammoniated and ureated," dentifrices were among the first dentifrices to skyrocket their sales through therapeutic claims. The early optimism was based on preliminary investigations. Although these early results were suggestive, there was little cause for jubilation when the longer clinical results were reported. If it were not for continued clever advertising the ammoniated dentifrices would probably have fallen of their own weight, long since.

The antibiotics have intrigued dentifrice manufacturers for several years, but since

permission for over-the-counter sales was withheld they have not become popular. Penicillin-containing dentifrices are available on prescription, but data from clinical studies here and abroad leave the questions of their effectiveness and safety in doubt. Few dentists write prescriptions for penicillin-containing dentifrices.

The latest splash comes from the makers of "anti-enzyme" dentifrices. Investigations of a *laboratory* nature showed that either sodium dehydroacetate or sodium lauroyl sarcinate might be effective in inhibiting acid production within the dental plaque for appreciable periods of time. On the basis of this evidence, one of the two pharmaceutical houses supporting the laboratory study marketed an "anti-enzyme" dentifrice with claims that it would give all-day "decay-acid immunity" after one brushing. This implies but does not claim decay prevention. The second manufacturer waited until the prepublication date issue of a university's bulletin containing a preliminary clinical report and then offered "lifetime" protection against decay.

The Council on Dental Therapeutics of the American Dental Association has not recognized any dentifrice as "therapeutic." Because the acceptable scientific papers on which the unacceptable advertising claims have been based are often published in the International Association for Dental Research's *Journal of Dental Research*, the officers of the Association issued a statement reading, in part, as follows:

> It is the hope of the officers of the Association that a truly therapeutic dentrifice will become available, but as yet they have seen no published evidence that warrants claims of great reductions in occurrence of dental caries through routine use of any dentifrice.

May the search for the therapeutic dentifrice continue, and, when and if it is found, may it be universally available and used. In the meantime, brushing the teeth immediately after eating offers the best hope for minimizing dental caries by hygienic measures.

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CANCER OF THE GALLBLADDER

GALLSTONES are found in a high proportion of patients with cancer of the gallbladder. Hence some have assumed that gallstones predispose to cancer. The statistical evidence seems, however, to have aroused some doubt in the minds of investigators in the Central Middlesex Hospital, London. In a publication in 1931, Graham stated that 8 to 10 per cent of all cancers arise in the gallbladder. Among 1,808 necropsies for malignant disease at the Cook County Hospital, Chicago, reported in 1941, 55 cases concerned cancer of the gallbladder and 62, cancer of the extrahepatic bile ducts. Other American investigators have emphasized the rarity of cancer of the gallbladder. Of 350,000 new patients who attended the Cleveland Clinic between 1932 and 1948, only 29 had cancer of the gallbladder which was verified by operation.

Now Cooke, Jones and Keech* have made a survey of cancer of the gallbladder in Great Britain. They have brought together the best documented series of cases reported in recent years. Only some 3 per cent of cases of gallstones were associated with cancer of the gallbladder. Gallstones are not produced as a result of dysfunction of the gallbladder due to cancer. The excess of women with cancer of the gallbladder is correlated with the excess of gallstones in women. The investigation reveals that cancer of the gallbladder accounts for under 1 per cent of all deaths from cancer in Great Britain. Among patients in whom a gallstone was found at necropsy, 12 per cent had died of complications arising from the gallstone. A review of the clinical histories of patients with gallstones suggested that it is impossible to forecast from the history whether the gallstone will ultimately cause death. Only a minority of gallstones subsequently caused difficulties. Because of these observations the authors conclude that, "It would seem reasonable to reserve surgery for patients who have developed troublesome

*COOKE, LORNA, JONES, F. AVERY and KEECH, MADELINE K.: Carcinoma of the gallbladder: A statistical study. Lancet 2:585-588 (September 19) 1953.

symptoms from their gallstones. The risk of cancer is not in itself sufficient reason for advocating cholecystectomy for symptomless gallstones."

Obviously this British point of view may not be concurred with by American surgeons. In this country removal of gallstones in many instances seems to be based largely on the x-ray evidence of their presence. Thus A. B. Small and C. A. Moyer, writing in Harrison's "Principles of Internal Medicine" say: "In view of the potential dangers of the asymptomatic stones (i.e., neoplasm, acute cholecystitis and common duct obstruction) it is now deemed preferable to remove such stone-containing gallbladders, provided that no contraindication to elective operation exists, and the surgeons within the locality are capable of performing the operation with a mortality rate of less than 1 per cent." The risk of mortality from the operation under modern surgical conditions seems to be slight. The decision of the surgeon would be made, therefore, on his estimation of the possibility of eventual harm from the gallstones as contrasted with the minute risk of operation under ordinary circumstances.

MORRIS FISHBEIN

REHABILITATION CENTERS

UNDER the auspices of the National Society for Crippled Children and Adults comes a compilation[1] on rehabilitation centers in the United States which includes information submitted by 40 rehabilitation centers for the First National Conference on Rehabilitation Centers which was held in 1952. Hardly any two of the centers are alike. They range from teaching centers which are parts of great universities to small curative workshops in which one or two therapists take care of outpatients. Some have medical directors; others do not have a medical director but depend on an attending physician for medical supervision. Some of the centers are financed by tax funds and others by contributions from their communities. One center for rehabilitation is financed by contributions made to a medical aid fund by employees and employers in a state workmen's compensation program.

The author of the compilation has divided the centers into six classes, depending on their scope and the kind of service that they render. The survey, with the exception of one center which serves only the tuberculous, is limited to those centers that serve several groups of people with disabilities. There are also a number of rehabilitation centers exclusively for the blind. Although two centers are old, namely, the Curative Workshop of Milwaukee (founded in 1919) and the Institute for the Crippled and Disabled in New York (established in 1917), by far the greater number have been established since World War II. Twenty-eight of the centers included in this survey were established since 1940 and nine of these were established since 1950.

Many changes have taken place in the concept of rehabilitation centers since such agencies were first established. Formerly physical therapy and occupational therapy were the main forms of service rendered. Later came speech therapy and psychosocial services. At present physical therapists with 222 positions are still the most numerous of employees of the centers and next most numerous are 117 occupational therapists. Physicians are third with 116 physicians, followed by 32 speech therapists, 26 counselors, 26 social workers and 14 psychologists.

A suitable definition of a rehabilitation center has not yet been established, the nearest being that "It is a facility for combining and making efficacious any or all parts of the process of rehabilitation." Other considerations of the subject indicate, however, what a rehabilitation center is not and the final definition will no doubt include statements as to what centers do now and also what they are not doing and should be doing. Such a definition will depend on the concept of a total rehabilitation process applied to those with any type of disability. Obviously many different services need to be integrated with the patient as the center of interest.

The new publication lists the various centers now available in the United States and gives important information regarding each

of them as to its work, participation of various professional groups in the community, support and similar data. Some of the centers have intimate connection with medical schools and universities; others are essentially referral offices for outpatients.

The final chapter in the book is entitled "Professional and community relationships in rehabilitation centers." It supplies data as to the multiple relationships necessary for adequate functioning of a rehabilitation center and indicates methods of organization to secure complete cooperation by all such established agencies in any community. Much information is, of course, also available from the Office of Vocational Rehabilitation in Washington, D.C., Miss Mary E. Switzer, Director.

MORRIS FISHBEIN

1. Redkey, Henry: Rehabilitation centers in the United States; a compilation of information submitted by 40 rehabilitation centers for the First National Conference on Rehabilitation Centers, December 1-3, 1952, under the sponsorship of the National Society for Crippled Children and Adults and the Office of Vocational Rehabilitation, U.S. Department of Health, Education and Welfare. Published and distributed by the National Society for Crippled Children and Adults, 11 South LaSalle Street, Chicago, Illinois.

POPULATION OF THE WORLD

The number of people in the world now is increasing at the rate of about 1 per cent a year. Twenty-five million people were added in 1953 at a rate of about 70,000 daily. With this rate of growth, in 1980 the world will have about 3.5 billion people which would be an increase of 46 per cent above the number in 1950. This amazing rate of growth is undoubtedly associated with the conquering of epidemic plagues and famines which have from time to time destroyed people faster than they were produced. Many sections of the world lack anything resembling actual statistics of births and deaths, particularly the countries of the Middle East, Asia, Africa and China. Incidentally the Soviet Union does not release such statistics.

Populations vary in their density from 4 in Oceania to 124 per square mile in Asia and 211 in Europe. In the Western Hemisphere the range is from 4 in Canada to 652 per square mile in Puerto Rico.

One wonders how long the present trend in the growth of the population will continue. Experts of the Population Reference Bureau in a recent report[1] point out that the limits are determined by the supply of food and other materials on which people depend. Already about one-half the people of the world are underfed and inadequately housed. Science has begun research to solve the problem by the development of synthetic foods of various kinds, including those produced naturally by yeast and weeds and those produced by chemical factories. Various artificially grown algae may supply dry material with a content of 50 per cent protein, making from 15 to 20 tons of the dry matter per acre. A pilot plant has been developed in which a few hundred pounds have been grown. At the present rate of study, generations will be required, as well as large amounts of money, to test the potentialities of this technic.

Robert C. Cook, who has written important contributions in this field, points out that in Japan and in Egypt at least governments are beginning to recognize the importance of the problem. In India a census was made in 1951 and a recent editorial in *The Statesman* of New Delhi urged some control over what was called "improvident maternity," that is, a birth occurring to a mother who has already given birth to three or more children. "Within the next 15 years the target should be," the editorial writer says, "to reduce the incidence of improvident maternity from its present level of 40 per cent to 5 per cent."

In the United States the problem is being discussed increasingly by both governmental and scientific leaders. Population problems are being openly discussed in relation to foreign policy, world trade and foreign aid. The United Nations has a section concerned with various aspects of the population problem and the first United Nations World Conference on Population is to be held in Rome in September 1954. Birth rates seem to be falling in Italy and Puerto Rico and altogether the situation is less depressing than it was when World War II ended.

MORRIS FISHBEIN

1. Population Bulletin. Population Reference Bureau, Inc. 10:1 (January) 1954.